KDIGO Controversies Conference on Improving CKD Quality of Care: Trends & Perspectives
Public Review Comments

As of May 30, 2022
Industry comments are highlighted in blue

Jessie Pavlinac - Oregon Health & Science University - Dietitian:
The below session should, if not already planned, include the vital role of nutrition intervention in earlier stages of CKD in progression of CKD and prevention of malnutrition.
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?

Ignacio Villanueva - Davita - Doctor / Physician:
Ok

Katy Wilkens - KDIGO Workgroup on CKD & Diabetes - Dietitian:
Would love to see more emphasis on nutrition therapy as a treatment for delaying progression of CKD. This treatment is very underutilized worldwide, either from lack of trained dietitians, lack of funding, or lack of understanding by care providers. For many poor people, changing their diet is an inexpensive, empowering way to affect the course of their disease. Sadly, few patients even get the opportunity to try. In the USA only about 6% of patients who see a nephrologist prior to needing dialysis are referred to a dietitian. If they are not seen by a nephrologist, the results are even more abysmal, only 0.03%.

Providers also tend to assume patients cannot follow a diet, which is certainly likely; if they don't receive any instruction on a diet, it's pretty difficult to follow. Happy to chat more and

happy to recommend some RD speakers for your program. Let's remember that prevention is much cheaper and effective than intervention. :-)

Darcy Weidemann - Childrens Mercy Kansas City - Doctor / Physician:
This is an important conference. I do think specifically mentioning scope of work and general applicability is important - is this intended to apply only to adult populations? What about infants and children, and young adults? Major advancements have been made in these areas related to children, including publication of the CKiD U25 equation, as well as various risk prediction methods, greater use of cystatin C in the pediatric populations, etc. I would hope that pediatric patients are well represented in the scope of the ensuing report, and suggest including of pediatric nephrologists at the conference.

Rafidah Abdullah - Malaysia - Doctor / Physician:
Good day, I am a practising nephrologist working in Malaysia. I am particularly interested in the module models of care. Following my Masters in Palliative Care from Kings College London (in 2019), I am slowly transitioning the model of CKD care in Malaysia with integration of palliative care. The evidence and recommendations are heading that way. Prevention and nondialysis therapy should be emphasized for LMIC countries.

Work and evidence-based research is currently on-going in Malaysia. I believe it will take a few years before it is eventually published. I would hope that KDIGO would strongly consider LMIC countries in its recommendations. We are lacking in healthcare personnel to follow the pre-existing guidelines and where most published research are from. Thank you.

Sanjay Kumar Agarwal - All India Institute of Medical Sciences - Doctor / Physician:
1. We should also include test for proteinuria, dipstick for over proteinuria, dipstick for microalbuminuria, point of care semiquantitative PCR or ACR as screening tests for primary care /screening level

2. We should include "Process of care of CKD" in different regions as that will guide for changes required in process of care of CKD for better outcome. Process of care is different in different countries and for different countries, actions required will be different.

Vladimir Tesar - Charles University Prague - Doctor / Physician:
Very important project. With the recent progress in the treatment of e.g. glomerular disease or ADPKD we are really approaching personalized treatment. This part of the programme is something new and for me of utmost interest.

Mary Callahan - Dallas Nephrology Associates - Nephrology Social Worker:
As a nephrology social worker of 35 years and now working in Nephrology Supportive Care, I would support the use of PROMs as listed in Models of Care, #2a, particularly frailty and fatigue with the CKD population as recommended in a previous KDOQI guideline (2002), yet not widely followed. In the 2002 recommendation quality of life screening was recommended in CKD patients. I support this and in late-stage CKD, the ESAS or IPOS might provide more specific info, particularly for patients over 65.

Smeeta Sinha - NHS England & Northern Care Alliance NHS Foundation Trust - Doctor / Physician:
An update to the 2012 CKD guidelines is welcome. The 'scope of coverage' document is appropriate and will hopefully enable a comprehensive update. I have listed some additional comments below which outline other areas which would benefit from review. Key gaps include:

- Role of genomics in diagnosis
- Point of care testing – LMIC but also increasingly adding value in other areas
- Risk prediction models in clinical practice – pros and cons at individual as well as policy level
- Screening and high-risk group recommendations
- A greater emphasis on CV outcomes especially heart failure throughout the updated document rather that CKD progression alone
- Organisational literacy as an enabler of increased patient education/awareness
- CKD in the setting of multi-morbidity (although this would make for an excellent KDIGO conference in and of itself)

Breakout Session 1: Diagnosis and Prognosis

Group 1. Models of Care
- Clear guidelines on value and implementation of biomarkers e.g., cystatin C particularly if being advocated as part of high-risk screening
- How does this CKD conference align with the CKD Early Identification and Intervention Toolkit that was co-produced by KDIGO and the ISN? https://kdigo.org/wp-content/uploads/2019/01/ISN_KDIGO_EarlyScreeningBooklet_WEB.pdf
- Screening/case-finding for CKD in general ought to be a key question within this section including population level systems/ lab systems to support case-finding
- Referral criteria for nephrology and role of integrated care – advice vs referral, asynchronous review. Harnessing digital innovation to identify at risk groups/those that may benefit from early review/referral

Group 2: Diagnosis and Classification

- Can and should available risk prediction models be incorporated into clinical pathways and decision making/policy e.g., KFRE > 5% prompt specialty review?
- Should risk prediction tools (KFRE/eGFR slopes) be provided to all patients and how should this be communicated to patients and carers?
- Communication of diagnosis and implications in general should be here - too many patents are informed of their CKD@ at the point of referral to nephrology at which point CKD is advanced. This is despite primary care providers being aware of early CKD many years previously. Patients have reported that they have been perhaps falsely reassured that there isn't anything to worry about until the point of referral
- I would like to see CV events as well as CKD progression throughout the document

Group 3: Innovative Diagnostics

- Need to include role of genomics in diagnosis of rare renal diseases particularly in paediatrics but also adults (Genome UK ai to embed into frontline clinical services)

Breakout Session 2: Disease Modification and Complication Management

Group 1: Models of Care

- Role of digital technologies, wearables in CKD monitoring e.g., BP monitoring.
- Current questions focus on a separation between primary and 'after' nephrology referral - consider models of integrated CKD care and population level systems for targeted intervention and shared-care supported by specialist advice & guidance.

Group 2: Individualized Pharmacotherapy

- Makes note of simple messaging to support education and implementation
- What can we learn from other LTC e.g., heart failure four pillars? Simple messaging improves adoption

Group 3: Polypharmacy

- Polypharmacy is often a result of due to multi-morbidity. Role of multi-professional MDT working in such cases including with patients.
- Alignment with heart failure particularly as there is synergy in treatments (RAASi, SGLT2i, MRA)
- Shared decision-making on prescribing (and investigation) with patients

I am the National Clinical Advisor for CKD to NHS England and would be grateful for the opportunity to join the conference proceedings. I would hope that I can provide valuable insight from our work in the UK.

Kelly Burdge - Mass General Brigham Salem Hospital - Doctor / Physician:
I think the biggest issue facing our profession is the misalignment of incentives. Patients come in with creatinines minimally changed, fearful of dialysis which is nowhere in their future. Then, patients with less means and multiple barriers to care have limited resources, caregivers don't "feel" their kidneys and keep being told things about it and then boom - they end up on dialysis. And insurance companies value a target BP (regardless of the patient and their beliefs, age or med side effects) and adequate KT/V- not anything the patient values. It leads to a lot of missed opportunities and unrealistic expectations.

Isaac Teitelbaum - University of Colorado - Doctor / Physician:
This appears to be very comprehensive. And I imagine that the topics I am about to suggest will likely be included in Group 3 of Breakout 1. Nevertheless, I write to ensure that they are:

1. Use of non-invasive transcutaneous techniques for measurement of GFR
2. Use of urinary ""omics"" to identify genomic or metabolic markers of various causes of CKD e.g. SLE nephritis, transplant rejection etc. "

Elizabeth Witten - Witten and Associates - Nephrology Social Worker, CKD Stage III:
This Scope of Work recognizes the challenge of low health literacy. How to assess and improve this should be a topic of discussion. The SOW states patient quality of life is important. Identifying and managing physical symptoms is an important aspect of health-related quality of life, but it's important to discuss how to identify barriers to emotional well-being and vocational goals so healthcare professionals can address them. Assuming that CKD covers all stages, the quality of care topic should include how to identify what the people with CKD value most. Fresenius has used Medical Education Institute's My Life, My Dialysis Choice decision aid, which currently helps people with CKD and ESRD see how each of the 7 types of dialysis fits with what they value most. MEI is revising this tool to include transplant and active medical management without dialysis. Quality of care discussions should also include how to address barriers to obtaining healthy and affordable food, medication, and kidney-protective treatments as well as treatments for kidney failure. When recommending medications, it's important to know that the two newer drugs that slow progression of CKD, Farxiga and Jardiance, retail in the U.S. for $500-$600/month or more. Those with CKD who are middle income and don't qualify for assistance programs may not be able to take those drugs even if their doctor prescribes them.

As I see it, the ultimate goal in CKD quality care should be to help those with CKD live full and productive lives.

Rumeyza Kazancioglu - Bezmialem Vakıf University - Doctor / Physician:
This has been designed satisfactorily.
Thank you.

Nertile Gjonaj - Doctor / Physician:
Perfect

Anna Köttgen - Freiburg University Germany - Doctor / Physician:
In the section on innovative diagnostics, would it make sense to add genetics in addition to e.g., imaging?
Or maybe genetics is not that innovative, and would also fit into the first section, with the question "how should patients be stratified according to parameters that are specific for the underlying kidney disease?"

Ali Gharavi - Columbia University - Doctor / Physician:
The CKD staging approach is very helpful as a stratification tool but also has the drawback of lumping together all different etiologies to kidney disease. Given recent advances in genomics and molecular profiling, it may be beneficial to also consider genetic testing to diagnose monogenic forms of kidney disease. Genetic testing is more widely available for clinical setting nowadays, and findings can have implications for clinical management, including therapy and selection of related donors for transplantation

Uwe Korst - Bundesverband Niere e.V / ERKNET - Patient:
To calculate the graft function (kidney function) the existing equations are not precise. All equations to calculate estimated GFR (eGFR) have the following lacks:
● MDRD (4 equations) are only valid from 18-70, study included 1625 participants only, is only valid for GFR >10ml/min to 60 ml/min
● CKD-EPI: much better
● Basis for the formulas is creatinine (serum)
● Age correction is not done (80-year-old healthy person has less then 100%)
● Muscle correction is not done
● Risk status
● Creatinine hat a blind area and has factors affecting the results like reduced muscle mass, Ingestion of cooked meed, malnutrition, Ketoacidosis and others
● How correct is eGFR with tubular diseases?

Summary:
Need to develop a better way to calculate the correct eGFR.

Beside medical support the scope of work should also include a section: What should a patient know to be adherent? What education/training is necessary?

a) regular training for patients should be improved (Online resources, patient materials, self checks, regular reminders e.g. via email, ...)

Background: general knowledge of patients about kidney is low
- what should I know about the kidney
- training on risk factors (see e.g. poster of NKF)
- training ""how do I keep my QoL""
- training ""what can I do to keep my kidney function for a long time""

b) mental health as a factor
Informing kidney transplant patients that their kidney/allograft is failing is associated with a range of emotions and has a significant impact on their future (see Table 1). Adapting to this new reality will be difficult for many and anticipating their psychological needs is an important role of the physicians team. The patitents identified mental health as a priority. Psychologycal support (checklist) should be a part of the visit.

c) 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice, many of the prevention scenarios apply to kidneys:
https://academic.oup.com/eurheartj/article/42/34/3227/6358713

d) Model of care
the need for multidisciplinary (MDC) patient integrated care clinics particularly for this complex patient group.

Sources:
21. SM, Hsiao LC, Ting IW, et al Multidisciplinary care in patients with chronic kidney disease: a systematic review and meta-analysis. European journal of internal medicine. 2015;26(8):640-5.
22. Valentijn PP, Pereira FA, Ruospo M, et al. Person-centered integrated care for chronic kidney disease: A systematic review and meta-analysis of randomized controlled trials. Clinical Journal of the American Society of Nephrology. 2018 Mar 7;13(3):375-86.

Magdalene Assimon - University of North Carolina at Chapel Hill - Pharmacist (PharmD) and PhD-trained researcher:

Breakout session 2 – Group 1: Models of Care

*Before, landing on an "optimal" model of CKD care it is important to recognize that fragmentation of care is a barrier to optimal patient management (Sloan et al. Semin Dial. 2020 Nov;33(6):440-448) in the U.S. and other countries. While the Sloan article is focuses on care fragmentation as a barrier to optimal ESKD care, the concepts discussed apply to patients with non-dialysis-dependent CKD and transplant, and the full age spectrum. An important point noted by Sloan et al. that would be great fodder for group discussion: a "lack of coordinated care affects quality of care in every domain and likely has an impact on patients' quality of life and life expectancy as well. Efforts to improve care coordination should be directed toward greater involvement of the PCP in the care of patients with CKD and ESKD, greater electronic interoperability between health systems, and development of new models of care that are truly patient-centered."

Breakout session 2 – Group 2: Individualized Pharmacotherapy

*Discussing barriers to receiving "disease-modifying" medications across the world as outlined is very important. In the U.S., for example, cost and getting insurance companies to cover drugs such as SGLT2i and finerenone are challenging. It's likely that this is also the case in other areas of the world as well.

*Related to the above point, a discussion of "pharmacoequity" is also important. For example, studies have shown that racial minorities in the U.S. are less likely to receive SGLT2i (Eberly et al. JAMA Netw Open. 2021 Apr 1;4(4):e216139). It will be also important to understand what pharmacoequity issues exisit related to prescribing "disease-modifying" medications outside the U.S. as well.

A relevant general commentary on the topic of pharmacoequity:
https://jamanetwork.com/journals/jama/article-abstract/278558

*An important topic worth discussing related to individualizing pharmacotherapy is the importance of drug dosing and associated unique medication safety concerns 1) as patients' CKD progresses, 2) as patients transition to dialysis, 3) when patients with non-dialysis-dependent CKD and dialysis-dependent receive a transplant, etc.

Breakout session 2 – Group 3: Polypharmacy

*In the general population concerns related to polypharmacy are chiefly focused on the elderly. However, in the setting of kidney polypharmacy is a concern regardless of age (e.g., younger and older adults, as well as pediatric patients). For all of the outlined discussion topics with will

be important to discuss each of the points as they related to patients with kidney disease across the age spectrum. Are there special considerations that are unique to specific age groups?

*Because of their extensive level of polypharmacy, patients with kidney disease, are at an increased risk of drug-drug interactions. Much of the focus of drug-drug interactions has been on describing the use on potentially dangerous medication combinations and less attention has been paid to evaluating their clinical consequences. What are effective strategies for detecting and managing potentially dangerous drug-drug interactions?

*It is important to consider medication risk-benefit. While specific medications and medication combinations may and increase risk of adverse outcomes, some patients may be willing to accept these risks for the potential benefits. Individualization of care should be a priority.

Elliot Tannor - Komfo Anokye Teaching Hospital - Doctor / Physician:
Low and low middle income countries have less resources and nephrology workforce making the diagnosis and management of kidney disease a daunting task. It will be great for the controversies conference to come up with strategies to aid the diagnosis and management in resource poor settings and the use of essential algorithms to aid task-shifting in areas without nephrologists.

Nuria S. Perez Romano - Doctor / Physician:
Poli pharmacy is one of the most hot topic. Failure of treatment, hospital admission many times are related to poor compliance.
Factor as no insurance covered medications, number of tables, low educational level about CKD and why patient will get benefits of the medication, psychological conditions not treated as depresión often in chronic patient, no family support special in patients with disabilities or elderly.
Moreover, lack of clinical pharmacist to help with the right prescription are some of the most common issues.
Multidisciplinary approach; nephrologist, family physician, renal nurse, social worker, dietician (also food- medication interaction is important), clinical pharmacist and psychology if need are the cornerstone of treatment of CKD patient. Also social media, religious referents, government institutions support is relevant.

Laura Sola - Hemodialysis Unit CASMU-IAMPP - Doctor / Physician:
At the Breakout Session 2: Disease Modification and Complication Management
Group 1: Models of Care
1. What is the optimal model of CKD care?

Is it possible to add a question regarding: Is there a possible role for telemedicine in the interaction of the general practitioner with the nephrologist in the care of kidney disease?

Patricia Abreu - Federal University of São Paulo - Doctor / Physician:
Group 1: Models of care
I would like suggest including the Charlson comorbidity index (PROMs). Thank you for the opportunity to participate in this discussion

Kyle Ashton - Travere Therapeutics:
Three suggestions:
1) consider more of a focus on earlier and broader detection of kidney disease
2) possibly include utility and collection of data, especially home monitoring and apps, and patient access to data
3) consider including patients in the conference, especially in the section concerning patient reported outcome measures (PROMs)

Johannes Mann - kfh kidney center - Doctor / Physician:
- Prognostication: suggest to focus on added value (or power for re-classification) of novel markers of CKD progression, for example supar or dkk3 over and above traditional markers that make up the canadian/us KFRE, kidney failure risk equation (short and extended versions). New markers may be great but if precision of traditional parameters is high, additional value of new markers may be negligible. In addition cost is a consideration.
- Long-term care and proms: suggest to involve CKD patients in these discussions. Avoiding dialysis appears to be of great importance to patients, in addition or over survival; the latter is particularly clear from a perspective of kidney transplanted patients that approach re-dialysis. That patient perspective is not reflected by the increase of mean or median eGFR at start of chronic dialysis in many countries in recent decades, which appears to be directed by the US system to refund dialysis if eGFR is below 15, an arbitrary threshold.
- Considering cost: You may consider to stratify recommendations into "implement in all", "implement if plenty of money available for health care" and something in between. Not an easy discussion. For example in our country, urine measurement of protein is much cheaper than albumin though.
- Research needs: in (advanced) CKD there are many research questions that could be answered by large and simple trials at low cost. For example in CKD-MBD there is only 2 or 3 such large trials addressing proms, like bone fractures, fall, pain etc while we have abundant data on lab parameters. I'd suggest that this conference identifies such research questions that can be answered by the nephro community with public support. The pharma industry will not help here or only to a very limited extend.

WendySt. Peter - University of Minnesota - Pharmacist:
I would suggest that 1 question be added/integrated into Breakout session 1: Group 2

Which factors should be considered when choosing between mGFR or mCrCL and eGFR estimating equation or marker for estimating GFR when classifying a patient for drug-related decision-making.

I would suggest the following question be added/integrated into to Breakout Session 2, Group 1

How can we strengthen clinical care models to ensure that a patient-centered approach is utilized for medical and medication-related decision-making?

Breakout session 2, Group 2

I would suggest that the following question replace current Q1

How can we ensure that each patient with kidney disease receives evidence-based patient-centered medication management to ensure their medications are indicated, safe and effective and that they can take their medications as intended?

I would suggest the following question replace Q3

What are the enablers and barriers for implementation of optimal medication management in patients with CKD: 1) across settings and, 2) available resources?

I would suggest the following question replace Q4.

What areas of research remain unanswered to address challenges/barriers to optimal patient-centered medication management (safe, effective medication use) in patients with CKD?

Pierre Delanaye - CHU Sart Tilman, Liège - Doctor / Physician:
The absence of an age adapted definition of CKD is discussed for many years, and is still debatable (Delanaye P, JASN, 2019, p1785).

The race-free CKD-EPI equation is now recommended by ASN and NFK. The main question remains about the applicability of this equation outside USA.

Paul Stevens - East Kent Hospitals University NHS Foundation Trust - Doctor / Physician:
1. What about point of care tests? 2. How much can the existing evidence in CKD derived from defined populations be extrapolated? ie what is its generalisability?

Edwina Brown - Imperial College Healthcare NHS Trust - Doctor / Physician:
CKD can be part of ageing and result from other comorbidities. In many kidney function, although poor, is stable and the least of their problems and there is no benefit to that person being under the care of yet another specialist team with more investigations and clinic visits, never mind the risk of polypharmacy - and increased healthcare costs. More consideration therefore needs to be given to overall health status, age and prognosis.

Antonio Garreta - Bayer - Biochemist:
Please see our comments in the draft agenda:

Group 2: Diagnosis and Classification

- How to involve primary care in Albuminuria detection, diagnostics and its clinical implications
-How to prevent CKD in the elderly population? Are current available drugs an option?

Group 3: Innovative Diagnostics

-Should the medical community consider other new methods for CKD detection (genomics, proteomics etc)
- Which are the most reliable biomarkers to detect inflammation and fibrosis?

Breakout Session 2: Disease Modification and Complication Management
Group 1: Models of Care

how are different CKD slopes (40% vs 57%) accepted my the medical community and payers?
Which is the best combined enpoint to determine kidney function loss?

Group 3: Polypharmacy

-In case of combination of drugs, how can the medical community work with Patients to increase adherence awarness?
-CKD is often assympotmatic what are the critical medications to be taken?

Overall comment: We would welcome the inclusion of the Finerenone data as the data has demonstrated a kidney function preservation.
-Which are the role of the new non-steriodal MRA in CKD prevention?

Wenjun Ju - University of Michigan - Research scientist with PhD on molecular biology:
I have worked in the chronic kidney disease filed for over 20 years, focusing on prognostic, predictive and pharmacodynamic biomarkers. systems biologist
For group 1: Measures of Glomerular and Tubular Function-topic number 3, I would also like to hear discussions on: Taken the expression/localization of the factors in the kidney compartments and kidney cell types into consideration, understand where is the source of the factor and what are the possible confounding factors.
For group 2- Diagnosis and Classification- topic number 2, I would also like to hear discussions on: How to accurately measure albuminuria, how to minimize the variation of the albumin measurement (or other markers) that may not directly associated kidney function, for example: circadian rhythms, day-to-day variations etc.
For Group 3: Innovative Diagnostics, I would also like to hear discussions on:
How about prognostics?
Can circulating and urinary molecular biomarkers enhance the quality of clinical care delivered for CKD?
Patient involvement: urine collection and assays at home to monitor CKD progression?
The kidney precision medicine project and impact on CKD.

Gregorio Obrador - Universidad Panamericana School of Medicine - Doctor / Physician:
I have a few suggestions regarding models of care:
1) Importance of patient education for improving clinical outcomes
2) Integration of clinical decision tools and AI into electronic charts to improve clinical care delivery
3) Other PROMs: pain, sleep disorders"

Kunitoshi Iseki - Nakamura Clinic, Okinawa - Doctor / Physician:
Current problems in Japan related to early detection of CKD are
1) Albuminuria testing is only reimbursed for early stage of DKD,
2) Participation rate of the general screening (Specific Health Check Program) is about 50% of the target population (age 40 to 74 years). "CKD" is still not popular as "metabolic syndrome".
3) Clinically significant slope of eGFR change and/or decrease in proteinuria (albuminuria) are not clear for Japanese. Therefore, introduction of new drugs for CKD treatment is delaying.
For CKD treatment 1. HIF-PHI has been used for the past 2 years. It is interesting to see the impact on the prevention/ retarding the progression of CKD.

Michael Reiner - numares Group Corporation - Diagnostic Manufacturer:

I am submitting comments on behalf of numares Group Corporation. We appreciate the opportunity to comment and for opportunities to collaborate on this important topic. Please note: We can also provide these comments via Word Document as formatting of this text may be off copying into this online form.

Numares Response to KDIGO SOW on:
Improving CKD Quality of Care: Trends and Perspectives KDIGO Controversies Conference

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?

1.1. If asking what factors should be considered when choosing between GFR estimating equations, it is appropriate to define the term “factors” in more detail. In fact, it can mean: a) clinical criteria or b) mathematical constants that are used in the eGFR equations. With that said, it is our belief that most nephrologists are choosing an eGFR equation which is offered by their local services in clinical chemistry and because this is the practice they have followed for many years. The large numbers of different equations – all aiming at improving analytical accuracy – which have been published over the last 65 years and which were followed by many publications may have also irritated general practitioners and other non-nephrologists. Moreover, there are still open questions on GFR estimating equations that remain to be solved. The question is have all equations based either on eGFRcrea or eGFRcys alone or in combination reached an endless loop which indicates that their potentials have expired. However, this does not mean that they are no longer useful in clinical nephrology because they will remain the backbone for measuring eGFR by adding further biomarkers to improve both accuracy GFR measurement and interpretation of CKD stages. To summarize, this is our main concept (1,2).

Glomerular filtration rate (GFR) is generally accepted as the best overall index of kidney function in health and disease. The KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease recommends using serum creatinine and a GFR estimating equation for initial assessment of GFR. As such, eGFR is now an essential part of

standard of care to verify and classify CKD. Although in use for decades, the methods available for eGFR with endogenous markers (e.g., serum creatinine, cystatin C) still present important drawbacks (3, 4). All endogenous filtration markers also have non-GFR determinants (3). Additional limiting factors include the analytical determination of the substance itself (5-7), substances interfering with marker quantification (8), as well as non-glomerular filtration determinants, such as synthesis, tubular reabsorption, secretion, and extra-renal elimination. All this leads to substantial analytical bias and increased analytical imprecision of equations to estimate eGFR (3-5). Over 70 different equations have been developed to estimate glomerular filtration rate based on creatinine and/or cystatin C levels (9). However, the eGFR values resulting from these equations often differ from mGFR (the gold standard, see below) by ±30% or more. And, depending on the chosen equation, studies have shown that as many as 30-60% of patients are misclassified by CKD stage (9).

An approach that reflects both the glomerular filtration rate and CKD-associated renal dysfunction may be a solution to these deficiencies in certain patients. Such an approach requires the quantification of several renal biomarkers with high precision and accuracy. To avoid increasing analytical costs associated with multiple single biomarker assays, the use of nuclear magnetic resonance spectroscopy (NMR) as a multiplex analyzer capable to precisely quantify multiple unlabeled metabolites in a simultaneous physical measurement might be of consideration. NMR derived concentrations of creatinine, myo-inositol and valine in combination with an additional measurement of serum cystatin C was recently reported to accurately determine GFR and kidney function especially in the presence of confounding clinical factors (1, 2). The complex interplay of the four metabolites, which complement each other to mitigate individual weaknesses and enhance their contribution to overall clinical value, represents a physiologically more complex and therefore more elaborate way of using biomarkers. The concept of estimated GFR based on NMR metabolomics (eGFRnmr) expands the previous approach to combine metabolites into a panel to correlate with mGFR (10-12) more closely.

It is our belief that eGFRnmr is innovative because as an untargeted metabolomics approach is not restricted to the currently available biomarkers but could be further extended in specific use cases. Meanwhile, targeted approaches are restricted to the metabolites they target for and cannot be easily extended.

The concept is based on the idea to use the most robust, accurate and useful eGFRnmr technology by using a minimum of metabolites which can be easily applied to all people. This concept does not require different series of new test variations and variable biomarkers that must be specifically used in different groups of patients (according to etiologies, clinical

pictures, histologies, drug treatments, etc.) to drive personalized kidney care. The concept of eGFRnmr is innovative and allows creativity and complex systems thinking. In our first publication we described four markers: creatine, myoinositol, valine, and dimethyl sulfone. (1) In our second publication we replaced dimethyl sulfone by cystatin C (2). This is in line with KDIGO recommendation to add cystatin-C to creatine. This addition supports our hypothesis to add cystatin-C, but at same time, both publications show that four biomarkers are even better measures of eGFR than two biomarkers. Based on the strength of the four biomarkers used for measuring eGFR, our test opens the diagnostic pathway for identifying also new markers reflecting GFR stage associated co-morbidities. However, these new markers will have to be identified in selected cohorts of patients having the same stage of GFR but differing in the respective co-morbidity such as cardiovascular symptoms and signs. In our 1st publication we had named it “molecular phenotyping by matched sample sets”. It is our belief that this innovation will in the future positively contribute to personalized treatment in patients with CKD.

Accurate and precise eGFRnmr results will aid clinicians in assessing patient kidney function and will increase the trust of patients into the grading schedule of CKD stages. The resulting increase of doctor adherence to diagnostic and therapeutic guidelines and of patient compliance to medical recommendations may improve patient outcomes and reduce costs.

2. What factors should be considered when selecting a marker for estimating GFR, e.g., serum creatinine versus cystatin

It is our impression that the combination of eGFRcrea and eGFRcys is regarded as being the most accurate way of estimating from one serum sample (12) because eGFRcreat equations alone are associated with significant bias and imprecision resulting in false-high and false-low test results. However, currently only an isolated decreased eGFR <60 ml/min/1.73m² or less diagnosed based on an eGFRcreat 45-59 ml/min/1.73 m² (G3a) or less, no albuminuria, is subjected to confirmatory testing by measurement of an alternative endogenous filtration marker like cystatin C or a measured clearance. This group represents 3.6% of the US population and 41% of people in the US estimated to have CKD based on eGFRcreat and urine albumin-to-creatinine ratio (ACR) alone (10), and there has been substantial controversy over whether these persons have CKD or if they are over diagnosed.

On the other hand, there is substantial risk of underdiagnosis in patients presenting with isolated decreased eGFR based on an eGFRcreat 60-75 ml/min/1.73 m^2 without albuminuria or other manifestations of kidney damage. Hence, confirmation of decreased eGFR by measurement of an alternative endogenous filtration marker or a more invasive clearance measurement is warranted.

In addition to creatinine and cystatin (CysC), alternative filtration markers were recommended in specific circumstances where GFR estimates based on SCr and CysC are thought to be inaccurate and when decisions depend on more accurate knowledge of GFR, such as confirming a diagnosis of CKD, determining eligibility for kidney donation, or adjusting dosage of toxic drugs that are excreted by the kidneys (10).

New equations were recently introduced to estimate glomerular filtration rate (eGFR), making use of serum creatinine and/or cystatin C in combination with age and sex, but without race (14). However, simply removing race does not inherently also remove the disparity in the estimation of GFR in black participants compared to non-black participants (14). Therefore, further efforts are needed to allow fair evaluation of eGFR, independent of race, age and sex, especially in the context of serious patient conditions. Additional biomarkers, complementing creatinine and/or cystatin C, could allow for a more comprehensive, accurate and fair eGFR estimation.

It is our belief that these considerations warrant new ways of complex systems thinking before allowing new recommendations for GFR estimation. It has previously been shown that the addition of further metabolic biomarkers as a complement to creatinine and/or cystatin C can improve GFR estimation performance (1). The role of a decrease of valine serum concentration was discussed by us in relation to measurements of eGFRnmr (1). In CKD, the diseased kidneys do not only cause an accumulation of those substances in the serum which must be eliminated by the urine, but they also lead to a decrease in the production of vital substances thus, resulting in a decrease in serum concentration. We conclude that valine may play a different role in measuring GFR than creatinine and cystatin C.

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?

It is our belief that GFR thresholds for diagnosis or staging of CKD must be stratified according to patient characteristics other than age or sex. These characteristics include etiology of the

disease, clinical status of the patient (e.g., nephrotic vs non-nephrotic) and histology (vascular, glomerular, interstitial, postrenal damage).

Albuminuria thresholds for diagnosis or staging of CKD should not be stratified according to patient characteristics, however, the test for albuminuria must be highly sensitive and specific. Total protein is not fulfilling these two criteria. We believe albumin as glomerular marker and alpha-1-microglobulin as tubular marker must be measured and the result must be referred to urinary creatinine concentration.

2. How should patients be stratified according to parameters that are specific for the underlying kidney disease?

A major foundation of the KDIGO guideline is that CKD classification and staging is influenced primarily by clinical prognosis. Abundant evidence has shown that accurate staging of CKD is a powerful predictor of clinical outcomes. These findings have been strongest for mortality and cardio-vascular disease (CVD) events (KDIGO guidelines, https://kdigo.org/guidelines). As such, improved accuracy, precision, and net reclassification improvement of novel eGFR equations represent an essential part of optimized medical care to verify and classify CKD. Improved bias and accuracy of improved equations utilizing more involved combinations of biomarkers in addition to serum creatinine and cystatin C will support decision making by minimizing underestimation of long-term GFR decline in CKD. Once a diagnosis of CKD has been defined, assessing CKD progression based on GFR classification ("CKD stage") is recommended. Changes in eGFR lead to changes in GFR classification, which defines CKD progression and CKD progression establishes the patient care plan. The KDIGO Guideline notes:
"Failure to recognize CKD results in neglect of its consequences and complications, and late referral of people with advanced CKD resulting in worse renal replacement therapy (RRT) outcome. […] Therefore, identification of people at earlier time points in the trajectory of CKD, with appropriate management and earlier referral of those who would benefit from specialist kidney services, should lead to both economic and clinical benefits ".
However, an increasing number of studies are noting populations in which measuring the rate of progression of CKD using conventional eGFR has been found inadequate (13). In 449 type 2 diabetic patients with mGFR and eGFR values obtained over a median follow-up period of 4.0 (1.8-8.1) years estimation formulas fail to provide any reliable estimations of GFR changes over time. Long-term GFR decline was largely and uniformly underestimated in the study group. Based on estimated baseline GFR and GFR changes over time, no patient was expected to progress to ESRD (defined as GFR of 15 ml/min per 1.73 m^2) over his/her own expectancy of life, whereas based on measured values a high proportion of patients was expected to reach this end point before the age of 80 years. Given the centrality of GFR in characterizing CKD

progression, much effort should be focused on novel methodologies and biomarkers to determine GFR more accurately and precisely and its changes over time.
The recently introduced GFR(NMR) equation showed superior performance in terms of accuracy and precision (1, 2). These findings suggest that using novel biomarkers in combination with CysC and SCr can lead to improved accuracy of GFR estimation, including CKD classification. These considerations warrant new recommendations for GFR estimation.

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?
The main reason for establishing the grading system of CKD was to create an easily understandable ranking list for risk prediction of renal and extra-renal comorbidities such as anemia, acidosis, osteodystrophy, growth failure, etc.
The endpoints should focus on the GFR value which is used to qualify a patient for being put on a waiting list for kidney transplantation. The placement of a patient in a CKD stage based upon eGFR will trigger specific treatments. Therefore, accuracy of staging is critical. eGFRnmr is a new and important tool to improve accuracy, helping to better stage, but more importantly help clinicians make improved treatment decisions.
b. How should we combine or weigh cardiovascular risks versus kidney related outcomes versus survival?
We believe that this is an important area for our future studies utilizing eGFRnmr plus new biomarkers which will have to be identified by comparing sera of CKD patients with and without severe cardiovascular morbidity.
c. How can we best integrate risk prediction into patient communication?
Non-adherence to diagnostic guidelines of physicians and non-compliance of kidney patients to treatment schedules belong to the main culprits for preventable progression of CKD. Since non-adherence and non-compliance are inevitable during medical care, we should ask: a. who is at high risk, b. why is the risk so high and c. how could it be reduced by better communication of risk factors. Patients loose trust in care givers if tests are unpleasant, invasive, expensive and if the results are inaccurate. Trusting the doctor and compliance to treatment are intricately linked feelings of patients. As eGFRnmr testing can be considered non-invasive and accurate it has the chance to improve the cooperation between nephrologists and their patients.

Group 3: Innovative Diagnostics
1. What novel diagnostic tools can improve the quality of CKD diagnosis and monitoring?
Apart from NMR spectroscopy (1,2) several other tools like ultra-performance liquid chromatography-tandem mass spectrometry assay (12) may be used.

2. Can innovative renal imaging procedures enhance the quality of clinical care delivered for CKD?

Not Applicable

3. What additional information is needed to utilize innovative renal imaging procedures to enhance the quality of CKD care?

Not applicable

4. Can measures of inflammation, fibrosis and, vasculopathy enhance quality of CKD diagnosis and clinical decision making

Not applicable

5. What is the perspective for the utilization of kidney biopsies in the future?
Most stakeholders, especially patients, would prefer to avoid biopsies. If the accuracy of non-invasive diagnostic testing improves, the need for biopsy may decrease.

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

All Not applicable

Group 2: Individualized Pharmacotherapy
1. What information is needed to prioritize disease-modifying medications to maximize the quality of care?

Drug dosing in patients with CKD depends on the stage of CKD to avoid over- and under-dosing. Adjusting the loading dose and the maintenance dosage of a potentially toxic drug to the CKD stage or the eGFR will reduce toxicity. In addition, therapeutic drug monitoring measuring drug concentration in the serum will help reducing toxicity and increasing efficiency of therapy.

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?

Not Applicable

3. What are the enablers and barriers for implementation of individualized pharmacotherapy in clinical practice to optimize quality of care in different resource settings?
The accuracy of eGFRnmr and the resulting correct allocation of patients to CKD stages will improve individualized therapy. This argument holds especially true for differentiation between stages GI and GII, between GIIIa and GIIIb) and between GIV and GV For example, while the speed limit on a highway may be 65 mph, enforcement is often not applied until a radar picks up speed above 74 recognizing the lack of precision in measuring both the speedometer and radar device.
4. What areas of research remain unanswered to address challenges to implementation of individualized pharmacotherapy across different resource settings?
There is a need for metabolomics when investigating both intrarenal morbidity and CKD induced secondary extra-renal morbidity in patients with CKD. There is also the need to identify the influence of independent extra-renal co-morbidity on CKD measurement in older patients.

The search for the “perfect” estimated GFR equation during these past 65 years has resulted in a type of endless loop. This circularity has led to an environment that stifles innovation and opportunities for creative solutions. We believe this is an opportunity to exit from the “black hole” of this endless loop to one that encourages new technologies and complex systems thinking.

Group 3: Polypharmacy
1. What is the impact of polypharmacy on CKD progression and patient-centered

outcomes?
Not applicable

2. Is there evidence that reducing polypharmacy in patients with CKD can improve the quality of care delivered and/or patient outcomes?
Not applicable

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?
This question must be discussed between nephrologists and toxicologists. It is important for nephrologists to know if used medications are interfering with the methods of measuring eGFR. In our recently accepted manuscript for publication in the Journal DIAGNOSTICS we described that substance interference with eGFRnmr was limited to 4/40 of the investigated substances (15).

4. What tools are needed for clinicians to safely address polypharmacy (including the practice of deprescribing)?
The tools must include not only accurate measurement of GFR, but also include the chances to identify the risks of multiple co-morbidities and polypharmacy. We conclude that all these chances are provided by eGFRnmr.

References
1. Ehrich J, Dubourg L, Hansson S, Pape L, Steinle T, Fruth J, et al. Serum Myo-Inositol, Dimethyl Sulfone, and Valine in Combination with Creatinine Allow Accurate Assessment of Renal Insufficiency-A Proof of Concept. Diagnostics. 2021;11(2).
2. Stämmler F, Grassi M, Meeusen JW, Lieske JC, Dasari S, Dubourg L, et al. Estimating Glomerular Filtration Rate from Serum Myo-Inositol, Valine, Creatinine and Cystatin C. Diagnostics. 2021;11(12).
3. Steubl D, Inker LA. How best to estimate glomerular filtration rate? Novel filtration markers and their application. Current opinion in nephrology and hypertension. 2018;27(6):398-405.
4. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. The New England journal of medicine. 2012;367(1):20-9.
5. Seegmiller JC, Eckfeldt JH, Lieske JC. Challenges in Measuring Glomerular Filtration Rate: A Clinical Laboratory Perspective. Advances in chronic kidney disease. 2018;25(1):84-92.

6. Guignard J-P. Postnatal Development of Glomerular Filtration Rate in Neonates. Fetal and Neonatal Physiology: Third Edition. 22003. p. 1256-66.
7. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: estimates, variability and pitfalls. Nature reviews Nephrology. 2017;13(2):104-14.
8. Topf JM, Inker LA. Measurement of glomerular filtration rate. Nephrology Secrets: Fourth Edition2018. p. 22-9.
9. Porrini E, Ruggenenti P, Luis-Lima S, Carrara F, Jimenez A, de Vries APJ, et al. Estimated GFR: time for a critical appraisal. Nature reviews Nephrology. 2019;15(3):177-90.
10. Stevens PE, Levin A, Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group M. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Annals of internal medicine. 2013;158(11):825-30.
11. Coresh J, Inker LA, Sang Y, Chen J, Shafi T, Post WS, et al. Metabolomic profiling to improve glomerular filtration rate estimation: a proof-of-concept study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2019;34(5):825-33.
12. Freed TA, Coresh J, Inker LA, Toal DR, Perichon R, Chen J, et al. Validation of a Metabolite Panel for a More Accurate Estimation of Glomerular Filtration Rate Using Quantitative LC-MS/MS. Clinical chemistry. 2019;65(3):406-18.
13. Gaspari F, Ruggenenti P, Porrini E, Motterlini N, Cannata A, Carrara F, et al. The GFR and GFR decline cannot be accurately estimated in type 2 diabetics. Kidney international. 2013;84(1):164-73.
14. Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. New England Journal of Medicine. 2021;385(19):1737-1749.
15. Fuhrmann M, Schwaeble Santamaria A, Scott R, Meeusen JW, Fernandes M, Venz J, et al. Analytical Validation of GFRNMR: A Blood-Based Multiple Biomarker Assay for Accurate Estimation of Glomerular Filtration Rate. Diagnostics. 2022; 12(5):1120.

Alberto Ortiz - IIS-Fundacion Jimenez Diaz - Doctor / Physician:

1. Discuss concept of CKD blind spot.
2. Group 3: Innovative Diagnostics, Discuss integration of genetic diagnosis into the overall patient workup. Relative role vs kidney biopsy in proteinuric kidney disease in the young.
3. define the diagnostic workup that allows to assign diagnoses of exclusion, such as hypertensive nephropathy. Discuss the possibility to make such diagnosis only after a complete etiology workup has been made and define such workup that may include genetic diagnosis. Discuss whether In the absence of such workup (that may not be indicated) cause should be labelled unknown.

4. Group 1: Models of Care. Who should be assessed for CKD by whom? ESC2021 on CV prevention: UACR+eGFR as starting step in CV prevention, at same level as serum glucose and cholesterol: everybody that has glucose or cholesterol assessed should also have UACR assessed?
5. Group 1: Measures of Glomerular and Tubular Function. Role of eGFR slopes in early detection of CKD/ CKD risk (i.e. before eGFR hits 60) "

Viviane Calice-Silva - Pro-Rim Foundation - Doctor / Physician:
The scope of work addresses most important aspects related to CKD identification, management and other aspects involving quality of life and PROMs. I was just wondering which educational tools or actions would also be valuable to be better explored and stimulated with the aim to improve CKD identification and improve knowledge related to CKD risk factors, earlier screening etc. I think it would be worthwhile to consider that as an additional strategy to improve CKD detection mainly in places where a Nephrologist may not be available. Thanks for the opportunity.

Angela Jones-Leone - GlaxoSmithKline - PhD, Medical Affairs Sr Director:
Thanks for the opportunity to submit comments. Please see GSK comments below under each sessions.

Breakout Session 1: Diagnosis and Prognosis, Group 2: Diagnosis and Classification

Question 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?

GSK Comment: In addition to the above, could the committee consider CKD complications (i.e., anemia) being discussed here?

Breakout Session 2: Disease Modification and Complication Management, Group 1: Models of Care

Question 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?

GSK Comment: Could the committee consider in the discussion CKD complications (i.e., anemia) given its impact on QoL?

Lori-Ann Fisher - UHWI - Doctor / Physician:
Overall great scope of work and excited about the prospects in discussing novel approaches to diagnosis and targeted treatment of CKD. May be challenging given the heterogencity in access to CKD care in different resource settings, and even racial and social disparities within high-income settings. I guess my question would pertain to how to address these factors and how do these factors influence clinical decision making. It is alluded to in the objectives. But how do we specifically guide and standardize policy in improving equity of care. Maybe specific objectives on this would be useful??

Helen Yeh - AstraZeneca
In response to KDIGO's invitation for feedback on the scope of work for the KDIGO Improving CKD Quality of Care: Trends & Perspectives Conference, we would like to share our comments on behalf of AstraZeneca. The scope of work appears very comprehensive and would like to make the following suggestions:

Section	Comment
Breakout Session 1: Diagnosis and Prognosis **Group 1:** Measures of Glomerular and Tubular Function 2. What factors should be considered when assessing how frequently to measure albuminuria in clinical practice?	We suggest including discussion of albuminuria testing disparities (eg. with vs without diabetes, racial differences) with a focus on closing gaps.
Breakout Session 1: Diagnosis and Prognosis **Group 2:** Diagnosis and Classification	There is a growing body of evidence demonstrating extremely low diagnosis rates in Stage 3 CKD[1-4]. We suggest including a discussion of how best to close this gap and what needs to be done to increase urgency across all relevant stakeholders in primary care (ie. PCPs, pharmacists, nurses, etc.) & secondary care (ie. endocrinology,

	nephrology, etc.). We also suggest addressing how to best integrate early diagnosis (ie. stage 3) into patient communication, with consideration given to lifestyle recommendations, patient empowerment, and treatment options.
Breakout Session 1: Diagnosis and Prognosis **Group 2:** Diagnosis and Classification 3. How can risk prediction guide individualized clinical care and treatment planning?	We suggest addressing differences in risk prediction and clinical care by stage of CKD (ie. stage 3 vs stage 3+), with consideration given to any recommended differences by care setting (ie. primary care vs nephrology) to optimize early intervention. Further, we suggest addressing the role of diabetes status in risk stratification and management, with the goal of disrupting prevailing clinical inertia for nondiabetic kidney disease. Reference(s): 1. Virgitti JB, Moriyama T, Wittbrodt ET et al. REVEAL-CKD: Prevalence of undiagnosed early chronic kidney disease in France and Japan [abstract and poster]. Presented at: ASN Kidney Week; November 4-7, 2021; Virtual. Poster #PO2337. 2. Sultan AA, Barone S, Kumar S et al. REVEAL-CKD: Prevalence of and patient characteristics associated with undiagnosed stage 3 chronic kidney disease [poster]. Presented at: ADA 81st Scientific Sessions; June 25-29, 2021; Virtual. Poster #998-P. 3. Schneider MP, Peach EJ, Barone S, et al. REVEAL-CKD: Prevalence of Undiagnosed Early Chronic Kidney Disease in Germany [poster]. Presented at Virtual World Congress of Nephology (WCN); February 24-27, 2022; Kuala Lumpur, Malaysia. Poster #WCN22-0472. 4. De Nicola L, Peach EJ, Barone S, et al. REVEAL-CKD: Prevalence of undiagnosed stage 3 chronic kidney disease in Italy [oral presentation] Presented at 59th European Renal Association (ERA); May 19-22, 2022; Presentation MO509
Breakout Session 1: Diagnosis and Prognosis **Group 3:** Innovative Diagnostics 1. What novel diagnostic tools can improve the quality of CKD diagnosis and monitoring?	In addition to novel diagnostic tools, we suggest addressing novel screening models and patient pathways intended to improve efficiency and care.
Breakout Session 2: Disease Modification and Complication Management **Group 1:** Models of Care 1. What is the optimal model of CKD care?	We suggest a discussion of recommendations for key specialties (ie. primary care, endocrinology, nephrology) that link appropriate screening & monitoring to clinical intervention, helping to address the growing clinical burden of CKD.
Breakout Session 2: Disease Modification and Complication Management	We suggest attempting to establish a consensus of which therapies should be considered foundational therapies as part of a comprehensive care regimen and which should be distinguished for risk factor management (eg. glucose control, lipid control). As part of this discussion, we suggest addressing therapeutic intervention for the

Group 2: Individualized Pharmacotherapy 1. What information is needed to prioritize disease-modifying medications to maximize the quality of care?	range of etiologies enrolled in recent CKD trials, including hypertensive nephropathy and glomerular diseases.[1,2] We suggest a discussion of risk management beyond just slowing progression to ESKD, taking in account premature death and CV events. The majority of patients with CKD will die or experience a CV event rather than progress to ESKD. Therefore, addressing the totality of risk should be a key tenet of comprehensive care for patients with CKD and newer therapies have demonstrated robust benefit in this respect. **Reference(s):** 1. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383(15):1436-1446. doi:10.1056/NEJMoa2024816 2. EMPA-KIDNEY Collaborative Group . Design, recruitment, and baseline characteristics of the EMPA-KIDNEY trial [published online ahead of print March 3, 2022]. *Nephrol Dial Transplant*. 2022;gfac040. doi:10.1093/ndt/gfac040
Breakout Session 2: Disease Modification and Complication Management **Group 2:** Individualized Pharmacotherapy 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?	We suggest a discussion of sequence and timing for initiation of newer therapies (ie. SGLT2is, MRAs) in the context of existing therapies (ie. RASi), with the goal of addressing clinical inertia in CKD management. Consideration should also be given to RASi (ACEi/ARB) optimization using the novel oral K^+-binders to treat RASi-induced hyperkalemia, rather than RASi down-titration/ cessation.[1,2] **Reference(s):** 1. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int.* 2020;98(4S):S1-S115. 3. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int.* 2021;99(3S):S1-S87.
Breakout Session 2: Disease Modification and Complication Management **Group 3:** Polypharmacy	We suggest consideration be given to nephrotoxic medications that have the potential to accelerate loss of kidney function or common medications that need to be dose-adjusted based upon reduced kidney function.