# KDIGO Controversies Conference on Potassium Management
# Breakout Group Questions

**Group 1: Potassium Homeostasis**

1. What determines the internal distribution of potassium and internal potassium homeostasis? What is the role of aldosterone in mediating potassium uptake by extrarenal tissues? How does organic versus mineral acidosis affect potassium distribution?

2. What is the role of aldosterone in determining systemic potassium homeostasis? Is it primarily to regulate internal balance?

3. What is the special role of the distal convoluted tubule in systemic potassium homeostasis? How does the distal nephron sense potassium and regulate sodium-chloride co-transporter (NCC)? Does increased distal sodium delivery mediate the kaliuretic effects of diuretics? Are there novel channels that might represent future therapeutic targets?

4. How do therapeutic drugs affect these processes? Might knowledge of this new information provide insight as to the relationship between dietary intake and disease such as hypertension?

5. What is known about the diurnal variability in potassium homeostasis? What is the known about clock genes and how they might be involved in potassium secretion at the tubular level and in regulating aldosterone secretion?

6. What is known about the mineralocorticoid receptors particularly at extrarenal sites? This has relevance to new receptor blockers that are said not to cause hyperkalemia.

7. Is there a sexual dimorphism in kidney potassium homeostasis? What might be the clinical relevance of such a difference?

8. What is known about gastric renal signaling with regards to potassium homeostasis? What is the evidence favoring a 'feed forward' versus a 'feedback' system for potassium homeostasis?

9. What is known about potassium transport along the gastrointestinal (GI) tract? What is known about transport in each segment of the GI tract? Might differences in transport characteristics relate to differences in potassium lowering observed with new potassium-binding drugs? How does fecal potassium excretion change in patients with low glomerular filtration rate (GFR)?

10. How is this transport altered in the setting of advancing CKD? Does the use of inhibitors of the RAAS system affect GI transport and cause increased potassium in the setting of anuric patients on dialysis?

**Group 2: Potassium Intake & Epidemiology of Dyskalemias**

1. **Dietary potassium.** What are the dietary sources of potassium? Is high dietary potassium part of a healthy or an unhealthy eating pattern (e.g., association with Mediterranean or Dietary Approaches to Stop Hypertension (DASH) diets, Healthy Eating Index)? How does potassium intake vary around the globe (geographical, socioeconomic and cultural differences)? What other nutrients with salutary effects accompany diets high or low in potassium? How much do potassium additives add to daily potassium intake?

2. **Measuring dietary potassium.** How can dietary potassium intake be estimated or measured? What is the reliability and/or pitfalls of 24-hour urinary potassium excretion as a marker of dietary potassium intake in normal subjects and in those with CKD? How strongly do dietary and circulating potassium associate (in general and in persons with CKD)?

3. **Health effects of dietary potassium.** What are the health effects of dietary potassium in persons with normal function **and in persons with CKD**?

a. Dietary potassium (alone or in combination with dietary sodium) and blood pressure?
b. Dietary potassium (alone or in combination with dietary sodium) and cardiovascular event risk?
c. Dietary potassium and other outcomes (e.g., kidney stones, CKD progression, neuropathy, death)?
d. Does the source of dietary potassium (i.e., plant vs animal origins) have an effect on the clinical consequences of hyperkalemia?

4. **Dyskalemia incidence and determinants in healthcare.** How common are hyperkalemia and hypokalemia in healthcare (incidence)? What are the patient characteristics, comorbidities and medications that predict the risk of hyper- and hypokalemia (i.e., causes and risk factors)? Presuming kidney function as one of the strongest predictors, at what level of eGFR is renal potassium excretion significantly affected, such as to meaningfully modify circulating potassium?

5. **Modifying serum/plasma potassium with diet.** Is there any trial/interventional evidence that dietary potassium intake influences serum/plasma potassium in healthy persons or those with CKD? Is there any trial/interventional evidence indicating that changes in dietary potassium intake are associated with improved clinical outcomes (in healthy persons or those with CKD)? What is the evidence behind dietary potassium restriction recommendations for hyperkalemia prevention in CKD?

6. **Recommended dietary intake of potassium.** What is the current daily recommended intake and the usual potassium intake in the general population? How does this recommendation align with the evidence shown above? How does this recommendation and above evidence align with the classic dietary potassium restrictions for persons with CKD? How large is the problem of potassium additives for persons with CKD?

**Group 3: Hypokalemia**

**Hypokalemia in Patients without End-Stage Kidney Disease (ESKD)**

1. How should chronic hypokalemia be investigated in the stable, hypertensive patient?

2. How should chronic hypokalemia be investigated in the stable, normotensive patient?

3. How should acute hypokalemia be investigated in the emergency room? Can an overall treatment algorithm be developed to address Q1, Q2 and Q3?

4. How should hypokalemia in the stable, chronic hypertensive patient be treated (e.g., diet vs supplements vs medications)? At what level is hypokalemia life-threatening? How should acute, severe but undifferentiated hypokalemia be treated?

5. Who should diagnose and treat chronic hypokalemia? Does hypokalemia require specialist referral or can it be managed by primary care physicians? Is there any evidence on when magnesium should be measured and when it should be replaced?

6. Is there a threshold for low potassium levels that should lead to cancelling elective or emergency procedures?

7. Is chronic hypokalemia a risk factor for low GFR or progression of CKD?

**Hypokalemia in Patients Treated with Peritoneal Dialysis (PD)**

8. What is the prevalence of hypokalemia among PD patients?

9. What are risk factors for hypokalemia among PD patients?

10. What are the consequences of hypokalemia among PD patients, including peritonitis, obstipation, cardiovascular and residual kidney function, and is there any difference by chronicity of the hypokalemia?

11. What are the optimal treatment strategies (e.g., diet vs supplements vs medications)?

**Hypokalemia in Patients Treated with Hemodialysis (HD)**

12. Does end-of-treatment hypokalemia, or rate of change of serum potassium during dialysis, contribute to morbidity or mortality for patients on HD?

**Group 4: Chronic Hyperkalemia**

1. How should we define chronic hyperkalemia?
    a. Potassium threshold (how to define: e.g., > 5 mmol/L, > upper limit of normal, etc.) Should threshold be the same for all patients? (e.g., differences in normal kidney function vs low GFR vs ESKD patients; adults vs. pediatric patients, serum vs plasma; presence of comorbidities and etiology of CKD (e.g., DM, PKD, others); acute vs chronic; acid-base status)
    b. Absolute number of measurements vs. percent of measurements with abnormal values
    c. Need for chronic therapy (e.g., binder use; use of co-interventions that incidentally might reduce potassium, such as bicarbonate therapy, loop or thiazide diuretics; alteration in co-interventions that are otherwise indicated, such as RAAS blockade, sacubitril/valsartan, potassium-sparing diuretics?)
2. What is the ideal monitoring strategy for chronic hyperkalemia?
    a. Frequency of measurements, including after initiating drugs that lead to hyperkalemia or drugs that treat hyperkalemia.
    b. Methods of measurement (e.g., chemistry lab vs. point-of-care devices vs. need for other novel methods)

    How can chronic hyperkalemia be predicted?

    c. Causes and risk factors
    d. Risk scores for prediction (see also Q3e)
3. What is the significance of chronic hyperkalemia?
    a. Does chronicity confer protection from cardiovascular or other effects?
    b. Is there a potassium threshold for cardiovascular or other effects?
    c. Is there a threshold for high potassium above which should lead to cancellation of elective or emergency procedures?

d. Are there characteristics that modify the association of hyperkalemia with outcomes (e.g., CKD, left ventricular hypertrophy, and other electrolyte and acid-base disorders)?

e. Can the risk of hyperkalemia be assessed and individualized via use of prediction models, risk scores?

4. What are the risks and benefits for controlling chronic hyperkalemia?

    a. Impact on outcomes of interest (e.g., all-cause/cardiovascular deaths, malignant arrhythmias, initiation of kidney replacement therapy, hospitalizations, emergency room visits, patient-centered outcomes, satisfaction with diet, quality of life, gastrointestinal side effects)

    b. Impact on use of otherwise indicated medications such as ACEi/ARBs (see Q1c)

    c. Cost-benefit considerations

    d. Patient reported outcomes (e.g., patient perspectives on different strategies to control chronic hyperkalemia)

5. What are the options for management of chronic hyperkalemia? What is the evidence for the effectiveness of these in reducing hyperkalemia? What is the evidence for the effectiveness of following strategies in preventing adverse clinical outcomes?

    a. Treatment of exacerbating conditions (e.g., metabolic acidosis, hyperglycemia) and use of ancillary treatments with effect on serum potassium (e.g., diuretics)

    b. Is there any evidence on the safety and effectiveness of allowing a higher than normal range of potassium without treatment (a permissive strategy)?

    c. Discontinuation of relevant medications, effect of therapeutic compromises (e.g., decreasing dose or discontinuation of RAAS inhibitors in CKD/HF patients)

    d. Enhancement of renal potassium excretion (e.g., mineralocorticoid agonists)

    e. Decreasing potassium absorption (e.g., different types of binders)

    f. Special considerations (e.g., pediatric issues, LMICC issues)

    g. Is anything known about the patient perspective on different strategies for management of chronic hyperkalemia?

6. Special considerations in ESKD

    a. Modality considerations (HD vs. PD vs. frequent HD); role of residual kidney function/diuretic use; mass balance vs. electrophysiologic balance

b. HD bath composition: e.g., potassium, calcium, magnesium, bicarbonate; gradients vs. absolute values. Discuss specifics for LMICC where flexibility to adjust HD bath composition is limited.

c. Monitoring frequency (can also be discussed under Q2) and timing (e.g., pre-, post-, or interdialytic, day of week)

d. Liberalization of RAASi/MRA therapy

**Group 5: Acute Hyperkalemia and Hyperkalemia in AKI (acute kidney injury)**

**Epidemiology and etiology**

1. What is the prevalence of acute hyperkalemia in AKI and overall (e.g., in emergency department patients)?

2. What are the risk factors for development of acute hyperkalemia in AKI and overall (i.e., medications, comorbidities, etc.)?

**Diagnosis**

3. What are the optimal methods for measurement of acute hyperkalemia, and their accuracy (e.g., studies on accuracy of point-of-care testing versus laboratory [serology] measurement)

4. Are thresholds to define mild/moderate/severe hyperkalemia useful? Does symptomatology depend on tolerance of patients? If so, what potassium thresholds should be used to define:
    a. Severe hyperkalemia
    b. Mild/moderate hyperkalemia

**Management**

5. a. What arrhythmias are associated with hyperkalemia, and at what potassium threshold?
    b. What measurement properties from ECG could be used to predict clinically important acute adverse outcomes (e.g., arrhythmia)?

6. What are the indications for use of intravenous calcium/sodium-bicarbonate, insulin and glucose, β-agonists, loop diuretics in hyperkalemia?

7. What ECG changes warrant calcium administration?
    a. What is the evidence of the effectiveness of intravenous calcium to prevent arrhythmia in hyperkalemia?

8. What is the comparative effectiveness of the various agents for acute management of hyperkalemia to ***shift*** potassium:
    a. Timing of onset
    b. Duration of effect

9. What is the comparative effectiveness of the various agents for acute management of hyperkalemia to ***bind/excrete*** potassium (including dialysis):
    a. Timing of onset
    b. Duration of effect

10. What is the optimal algorithm for the management of hyperkalemia with respect to:
    a. Setting for management
    b. Treatment
    c. Ongoing monitoring (i.e., frequency and duration)
    d. Evaluation of current medications and potential changes in medications
    e. Indication for dialysis

11. Is anything known about the patient perspectives on emergency room visits for management of acute hyperkalemia?

**Consequences**

12. What are the adverse consequences of acute hyperkalemia, and at what potassium thresholds in relation to:
    a. Cardiovascular effects
    b. Non-cardiovascular effects

13. Messages for patients (and follow-up doctors) with acute hyperkalemia:
    a. Information concerning caution with concomitant medication use (e.g., aldosterone-antagonists, NSAIDs, etc.)