A Portuguese Modified Delphi Consensus on Quality Standards for Hyperkalemia Management in Portugal

Ana Natário[1], Irene Marques[2,3,4,5], Marco Mendes[6], Cátia Oliveira[7,8,9], João Porto[10], Ana Paula Silva[11], Joana Paixão[10,12], Paulo Araújo[13,14], Rodrigo Leão[15, 16], Luís Rodrigues[17], Renata Carvalho[18], Hugo Diniz[19]*

1. Nephrology Department, Unidade Local de Saúde Arrábida, Setúbal, Portugal;
2. Internal Medicine Department, Centro Hospitalar Universitário de Santo António (CHUdSA), Unidade Local de Saúde Santo António, Porto, Portugal;
3. Unidade Multidisciplinar de Investigação Biomédica, Instituto de Ciências Biomédicas de Abel Salazar (ICBAS), University of Porto, Porto, Portugal;
4. ITR- Laboratory for Integrative and Translational Research in Population Health, Institute of Public Health of the University of Porto, Porto, Portugal;
5. Centro Académico Clínico ICBAS-Santo António (CAC ICBAS-Santo António), Porto, Portugal;
6. Nephrology Department, Unidade Local de Saúde São José, Lisboa, Portugal;
7. Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal;
8. ICVS/3B's-PT Government Associate Laboratory, Braga, Portugal
9. Cardiology Department, Unidade Local de Saúde Braga, Braga, Portugal;
10. Internal Medicine Department, Unidade Local de Saúde Coimbra, Coimbra, Portugal;
11. Nephrology Department, Unidade Local de Saúde Algarve, Faro, Portugal;
12. Institute of Pharmacology and Experimental Therapeutics, Faculty of Medicine, University of Coimbra, Coimbra, Portugal;
13. Cardiology Department, Unidade Local de Saúde São João, Porto, Portugal;
14. RISE-Health, Faculty of Medicine, University of Porto, Porto, Portugal;
15. Internal Medicine Department, Unidade Local de Saúde São José, Lisboa, Portugal;
16. NOVA Medical School, Universidade NOVA de Lisboa, Lisboa, Portugal;
17. Nephrology Department, Unidade Local de Saúde Coimbra, Coimbra, Portugal;
18. Nephrology Department, Unidade Local de Saúde Braga, Braga, Portugal;
19. Nephrology Department, Unidade Local de Saúde São João, Porto, Portugal.

https://doi.org/10.71749/pkj.158

Abstract

Hyperkalemia (HK) is common in chronic kidney disease, heart failure, and other cardiovascular-kidney-metabolic (CKM) conditions, often impacting the use of guideline-directed medical therapies (GDMT). Despite scientific guidelines and available treatments, healthcare organization and care delivery also influence treatment patterns and quality of care for patients with HK.

This study aimed to develop consensus-based recommendations for HK management in Portugal, focusing on care organization, clinical practice, and treatment access, through a process that included regional multidisciplinary in-person meetings followed by a single-round modified Delphi panel. Afterwards, a focus group defined twenty-eight recommendations across three domains: A) healthcare organization and care pathways, B) clinical practice and therapeutic strategies, and C) access to potassium (K^+) binders. The online questionnaire was distributed to nephrologists (NE), cardiologists (CA), internists (IM), and hospital pharmacists (PH).

Ninety-nine participants completed the survey (IM: 38.4%, NE: 30.3%, CA: 25.3%, PH: 6.0%). Following a single Delphi round, all statements achieved high agreement (≥89%), with four unanimously approved. In domain A, structured care pathways, early clinical reassessment, and patient education were considered important. In domain B, panelists

Received: 29/07/2026 **Accepted:** 15/09/2026 **Published Online:** 22/09/2026 **Published:** -

* **Corresponding Author:** Ana Natário | ana.natario@chs.min-saude.pt | Nephrology Department of Unidade Local de Saúde Arrábida, Setúbal, Portugal

recognized the importance of integrated risk assessment, maintaining GDMT, and using new K^+ binders in acute and chronic HK. In domain C, agreement was highest, with full consensus on ensuring treatment continuity and simplifying administrative procedures delaying therapy initiation.
The need for standardized approaches, improved multidisciplinary coordination, and preventive HK management in Portugal was consistently supported. This national consensus provides a framework for developing quality standards to improve patient outcomes and promote consistent HK care across Portuguese healthcare settings.

Keywords: Angiotensin-Converting Enzyme Inhibitors; Chelating Agents; Delphi Technique; Heart Failure; Hyperkalemia; Patient Care Team; Polyamines; Polymers; Potassium; Quality of Life; Renal Insufficiency, Chronic; Silicates

INTRODUCTION

Hyperkalemia (HK) is a frequent and clinically relevant electrolyte disorder in patients with chronic diseases, particularly those with chronic kidney disease (CKD), heart failure (HF), diabetes mellitus, and hypertension, especially those on renin-angiotensin-aldosterone system inhibitors (RAASi).[1] Even slight elevations in serum potassium (K^+) are associated with an increased risk of cardiac arrhythmia, hospitalization, and mortality, making appropriate detection and effective management of HK crucial for the prevention of complications.[2,3]

In clinical practice, HK management is complex and often involves multiple medical specialties, including nephrology, cardiology, and internal medicine. Patients at risk frequently present with multiple comorbidities and experience high rates of care fragmentation, which has been associated with adverse outcomes, such as overuse of healthcare services and mortality rates. Over time, patients are managed across different healthcare settings,[4,5] including emergency departments, inpatient and outpatient settings, and primary care, highlighting the need for coordinated care pathways and clearly defined clinical protocols.[4] However, delivering integrated, multidisciplinary care remains challenging. Furthermore, variability in organizational structures, therapeutic approaches, monitoring strategies, and access to treatment options may lead to inconsistencies in patient management and potentially suboptimal outcomes.[6,7]

Recent advances in the pharmacological management of HK, particularly the availability of new K^+ binders (e.g. patiromer sorbitex calcium (patiromer) and sodium zirconium cyclosilicate (zirconium)), provide an opportunity to achieve effective serum K^+ control in patients in whom HK may arise either from the underlying cardiovascular-kidney-metabolic (CKM) disease or as a consequence of RAASi treatment.[8-10] By facilitating the sustained long-term maintenance of serum K^+ concentrations lower than 5.5 mmol/L, these agents may support RAASi optimization and reduce the need for dose reduction or discontinuation.[8] Nevertheless, the integration of these therapies into routine practice requires clear clinical guidance, defined patient selection criteria, and organizational frameworks that facilitate appropriate access and continuous care. While this is widely acknowledged by the main scientific societies[11-15] and healthcare professionals, there are no practical recommendations to serve as a backbone for the implementation of quality standards for HK management in the Portuguese healthcare landscape.

The present study aims to establish consensus-based recommendations for HK management in Portugal, focusing on the organization of care, clinical decision-making, and access to treatment, based on the insights of a multidisciplinary panel including experts in nephrology, cardiology, internal medicine, and pharmacy.

METHODS

Study Design

A modified Delphi process was carried out to develop consensus recommendations. Structured consensus methodologies such as the Delphi technique provide an approach to capture expert opinion in areas where clinical practice may vary or where evidence needs to be translated into practical recommendations.[6]

The methodology included three sequential phases (Fig. 1). Initially, eight multidisciplinary meetings were held in different regions of Portugal, including specialists in nephrology, cardiology, internal medicine, and hospital pharmacy. Discussions were structured through a SWOT analysis framework and focused on current practice, challenges, the intrahospital patient journey and opportunities for improvement in HK management, gathering insights to support statement development. In the second phase, a focus group of 10 experts (selected from participants pool in the regional scientific roundtables based on their clinical expertise and contributions to the discussions) was convened to review the extracted information and formulate a final list of 28 statements, organized into three domains: (A) healthcare organization and care pathways, (B) clinical practice and therapeutic strategies, and (C) access to K^+ binders. In a third phase, an online survey was conducted to capture expert opinion.

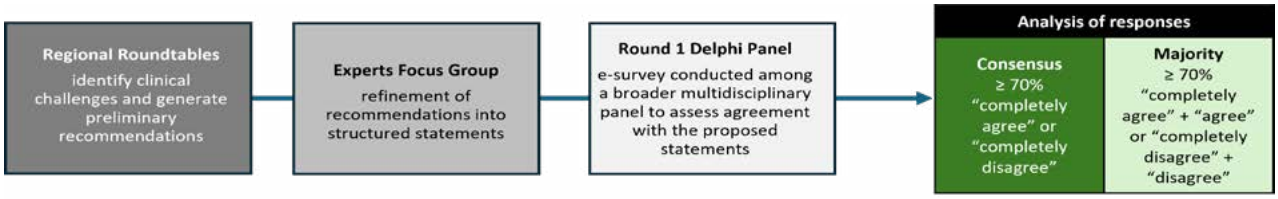

Figure 1. Methodology of the single-round Delphi-like panel.

Delphi Process

The final list of 28 statements (Table 1) was distributed to a mixed-specialty panel of healthcare professionals via an online questionnaire, between January 28th and March 18th, 2026. Experts were recruited using purposive sampling to include healthcare professionals with direct experience in HK management in Portugal. The panel comprised specialists in nephrology, cardiology, internal medicine, and hospital pharmacy, reflecting the multidisciplinary nature of HK care. Eligible participants were required to be in active practice and routinely involved in managing patients with HK. Level of seniority, geographic region, healthcare setting, and institutional diversity were also considered. A final panel of 50-100 participants was targeted, consistent with typical modified Delphi studies and sufficient to capture diverse expert perspectives. Accordingly, around 150 experts were invited to account for expected non-response and attrition across online survey rounds while preserving specialty balance. Hospital pharmacists only completed domain C.

Participants were asked to rate each statement using a four-point Likert scale. Formal consensus was defined as ≥70% of respondents selecting "completely agree" or "completely disagree." Majority agreement was defined as ≥70% selecting either "agree" or "completely agree." Responses were anonymous.

Table 1. Defined statements for the Delphi-like panel.

A. HEALTH CARE ORGANIZATION AND CARE PATHWAYS	
A1	The specialties of nephrology, cardiology, and internal medicine should agree upon and implement a single, standardized hospital protocol for the management of chronic hyperkalemia.
A2	Clinical protocols should define serum K^+ thresholds for intervention, intrahospital referral, and follow-up recommendations, based on risk stratification for hyperkalemia. The level of urgency and follow-up intervals should be adapted to the operational realities of each institution and specialty.
A3	Within the Local Health Unit, clear and standardized clinical pathways should exist between the emergency department, inpatient units, day hospital, and outpatient clinics for patients with hyperkalemia.
A4	Patients with recurrent hyperkalemia associated with underlying chronic disease, such as advanced chronic kidney disease (CKD), should be enrolled in regular follow-up protocols, aligning clinical guidance between the hospital setting and primary care services.
A5	Strategies should be implemented to facilitate early reassessment of patients with hyperkalemia, including systematic reassessment visits, open-access clinics, or day hospital services, in order to optimize therapeutic management and reduce clinical decompensations.
A6	Multidisciplinary teams and structured care programs for patients with cardiovascular-kidney-metabolic syndrome and hyperkalemia risk represent a key organizational strategy. These allow for comprehensive patient evaluation, optimization of guideline-directed medical therapies, and management of adverse effects and comorbidities, with a potential impact on reducing hospitalizations and mortality.
A7	Hybrid follow-up models, including telemedicine consultations and hospital-at-home programs, may be considered for selected patients at high risk of hyperkalemia, whenever available and clinically appropriate.
A8	Clinicians should educate patients (and/or caregivers) about the risks of hyperkalemia, recognition of signs and symptoms, dietary strategies, and precipitating factors.
A9	Pharmacy teams should have a formal role in medication reconciliation for patients with hyperkalemia, particularly during the transition from hospital care to primary care, ensuring continuity of access to prescribed therapies.
B. CLINICAL PRACTICE AND THERAPEUTIC STRATEGIES	
B1	Patients with CKD and/or cardiovascular-kidney-metabolic syndrome should be considered at risk for hyperkalemia based on an integrated clinical assessment, including: • CKD severity: estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2 and urinary albumin-to-creatinine ratio (UACR) >300 mg/g • Prior history of hyperkalemia • Diagnosis of diabetes mellitus • Diagnosis of heart failure (HF) • Treatment with renin–angiotensin–aldosterone system inhibitors (RAASi) • Baseline serum K^+ levels >4.5 mmol/L
B2	In acute hyperkalemia associated with acute kidney injury, assessment of kidney function should not rely on estimated GFR, given the limitations of this parameter in non–steady-state conditions.

B3	Chronic hyperkalemia is recommended to be defined as persistent serum K^+ ≥5.1 mmol/L in ≥2 laboratory assessments over ≥4 weeks (after excluding pseudohyperkalemia). Hyperkalemia should be classified as: • Mild: serum K^+ 5.1–5.9 mmol/L without ECG changes • Moderate: – serum K^+ 5.1–5.9 mmol/L with ECG changes, or – serum K^+ 6.0–6.4 mmol/L without ECG changes • Severe: – serum K^+ 6.0–6.4 mmol/L with ECG changes, or – serum K^+ ≥6.5 mmol/L without ECG changes
B4	Reduction or discontinuation of guideline-directed medical therapies in patients with CKD and/or HF due to hyperkalemia should be avoided whenever effective alternatives are available.
B5	Management of hyperkalemia should be proactive, with regular laboratory monitoring of serum K^+ in patients receiving potentially hyperkalemia-inducing therapies, particularly RAAS inhibitors.
B6	The use of new K+ binders in acute hyperkalemia may reduce the need for renal replacement therapy and should be incorporated into hospital protocols.
B7	The use of new K+ binders is clinically appropriate in the chronic management of hyperkalemia, when required to allow continuation of RAAS inhibitor therapy.
B8	New K+ binders should be preferred over traditional resins, due to their superior efficacy, tolerability, and safety profile.
B9	The choice between patiromer and sodium zirconium cyclosilicate should consider: • mechanism of action • safety and tolerability profile • time to achieve normokalemia • risk of hypomagnesemia • drug–drug interactions • storage requirements
B10	Patiromer may be considered for the treatment of hyperkalemia in the chronic maintenance setting, based on currently approved indications.
B11	Sodium zirconium cyclosilicate may be considered for the treatment of hyperkalemia in acute correction and/or chronic maintenance, based on currently approved indications.
B12	Based on recent scientific evidence, sodium zirconium cyclosilicate should be considered for the chronic treatment of hyperkalemia in adult patients with CKD stages 3–5, including patients with end-stage kidney disease or those enrolled in a regular hemodialysis program.
B13	In patients treated with sodium zirconium cyclosilicate who have pre-existing heart failure, particularly those in whom increased sodium intake may lead to fluid overload and decompensation, monitoring for signs of HF worsening is recommended and management should follow standard clinical practice.
B14	In patients treated with patiromer, serum magnesium (Mg2+) levels should be monitored regularly, and cases of hypomagnesemia should be treated with appropriate supplementation.
C. AVAILABILITY AND ACCESS TO NEW K+ BINDERS	
C1	Hospital dispensing of new K+ binders should ensure continuity of maintenance therapy between outpatient visits, avoiding treatment interruptions and unnecessary travel to the hospital pharmacy.
C2	The requirement for case-by-case approval by the Pharmacy and Therapeutics Committee (P&T Committee) for prescribing new K+ binders represents a barrier to therapeutic optimization. This process should be simplified and supported by hospital dispensing protocols, avoiding delays in treatment initiation for eligible patients.
C3	Whenever possible, on the day of the consultation, the hospital pharmacist should dispense the prescribed K+ binder and instruct the patient on administration, potential adverse effects, and relevant precautions.
C4	According to Order No. 10110/2024 of August 29, community-based dispensing (proximity dispensing) should consider new K+ binders as a strategy for the treatment of hyperkalemia, in order to improve adherence to guideline-directed medical therapies and reduce the risk of morbidity and mortality in patients with CKD and/or cardiovascular-kidney-metabolic syndrome.
C5	Within the proximity dispensing framework, community pharmacies will play a crucial role in medication reconciliation and in maintaining RAAS inhibitor therapy prescribed by the hospital treating physician.

RESULTS

A total of 99 healthcare professionals completed the Delphi questionnaire. Respondents were distributed across internal medicine (38.4%), nephrology (30.3%), cardiology (25.3%), and hospital pharmacy (6.0%). Most participants had been attending physicians for over three years (Table 2). Domains A and B were completed by clinicians only (n=93), whereas domain C additionally included hospital pharmacists (n=99).

Table 2. Distribution of healthcare professionals participating in the Delphi-like panel (N=99).

	Professional experience (N)			Total N (%)
	> 3 years	≤ 3 years	Residents in training	
Nephrology	22	7	1	30 (30.3%)
Cardiology	17	3	5	25 (25.3%)
Internal Medicine	22	10	6	38 (38.4%)
Pharmacy	-	-	-	6 (6.0%)

All 28 statements achieved majority agreement, defined as ≥70% of respondents selecting "agree" or "completely agree". Four statements additionally achieved formal consensus, defined as ≥70% selecting "completely agree". Given the uniformly high levels of endorsement across all domains, a second Delphi round was not considered necessary (Figs. 2-4, Supplementary Tables S1-S3).

Domain A: Healthcare Organization and Care Pathways

All nine organizational statements achieved majority agreement, with overall support ranging from 89% to 99% (agree + completely agree). Statement A8 (Fig. 2), recommending patient and caregiver education regarding hyperkalemia risks, symptom recognition, dietary measures, and precipitating factors, achieved formal consensus.

Statements supporting structured pathways between emergency departments, inpatient wards, day hospitals, and outpatient clinics (Statement A3; 98%) and regular follow-up protocols for recurrent hyperkalemia associated with chronic disease (Statement A4; 99%) received the highest majority agreement rates within this domain. Early reassessment strategies such as scheduled revisit pathways, open-access clinics, or day hospital models (Statement A5) also showed very high support (99%) (Fig. 2).

The creation of multidisciplinary programs for patients with CKM syndrome and hyperkalemia risk (Statement A6; 98%) and a formal role for pharmacy teams in medication reconciliation during transitions of care (Statement A9; 97%) were strongly endorsed. Hybrid follow-up models, including telemedicine and hospital-at-home programs (Statement A7), received slightly lower agreement (89%) (Fig. 2).

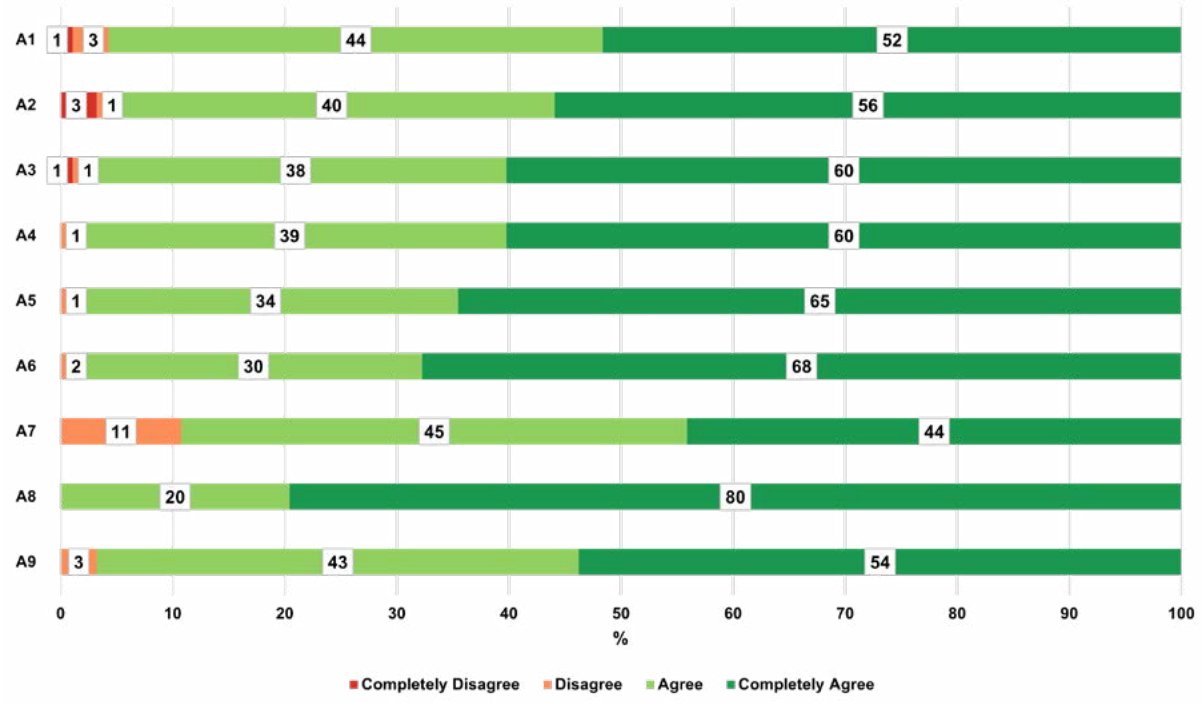

Figure 2. Overall characterization of statements (per %) from domain A – Healthcare organization and care pathways.

Domain B: Clinical Practice and Therapeutic Strategies

All 14 clinical statements achieved majority agreement, ranging from 90% to 99%. Respondents strongly supported integrated risk stratification for hyperkalemia in patients with CKD and/or CKM syndrome (Statement B1; 98%) and proactive laboratory monitoring in patients receiving K^+-raising therapies, particularly RAASi (Statement B5; 99%) (Fig. 3).

Statement B4, recommending avoidance of unnecessary reduction or discontinuation of guideline-directed medical therapies (GDMT) when effective alternatives are available, achieved 95% majority agreement. Additionally, Statement B6 reached formal consensus, indicating strong support that new K^+ binders in acute hyperkalemia may reduce the need for renal replacement therapy and should be incorporated into hospital protocols (Fig. 3).

High support was also observed for chronic use of new K^+ binders to enable continuation of RAASi therapy (Statement B7; 96%) and for preferential use of newer binders over traditional resins because of superior efficacy, tolerability, and safety (Statement B8; 97%) (Fig. 3).

Ninety-nine percent of the experts agreed that treatment selection among the new K^+ binders should consider the mechanism of action, time to normokalemia, safety profile, hypomagnesemia risk, drug interactions, and storage

requirements (Statement B9) (Fig. 3). Statements supporting patiromer for chronic maintenance (Statement B10; 92%) and zirconium for acute correction and/or chronic maintenance (Statement B11; 99%) were both highly rated. Notably, a higher proportion of respondents expressed total agreement with the statements relating to zirconium than with those relating to patiromer (62% vs 38%). Support for zirconium in advanced CKD and dialysis populations reached 97% (Statement B12) (Fig. 3).

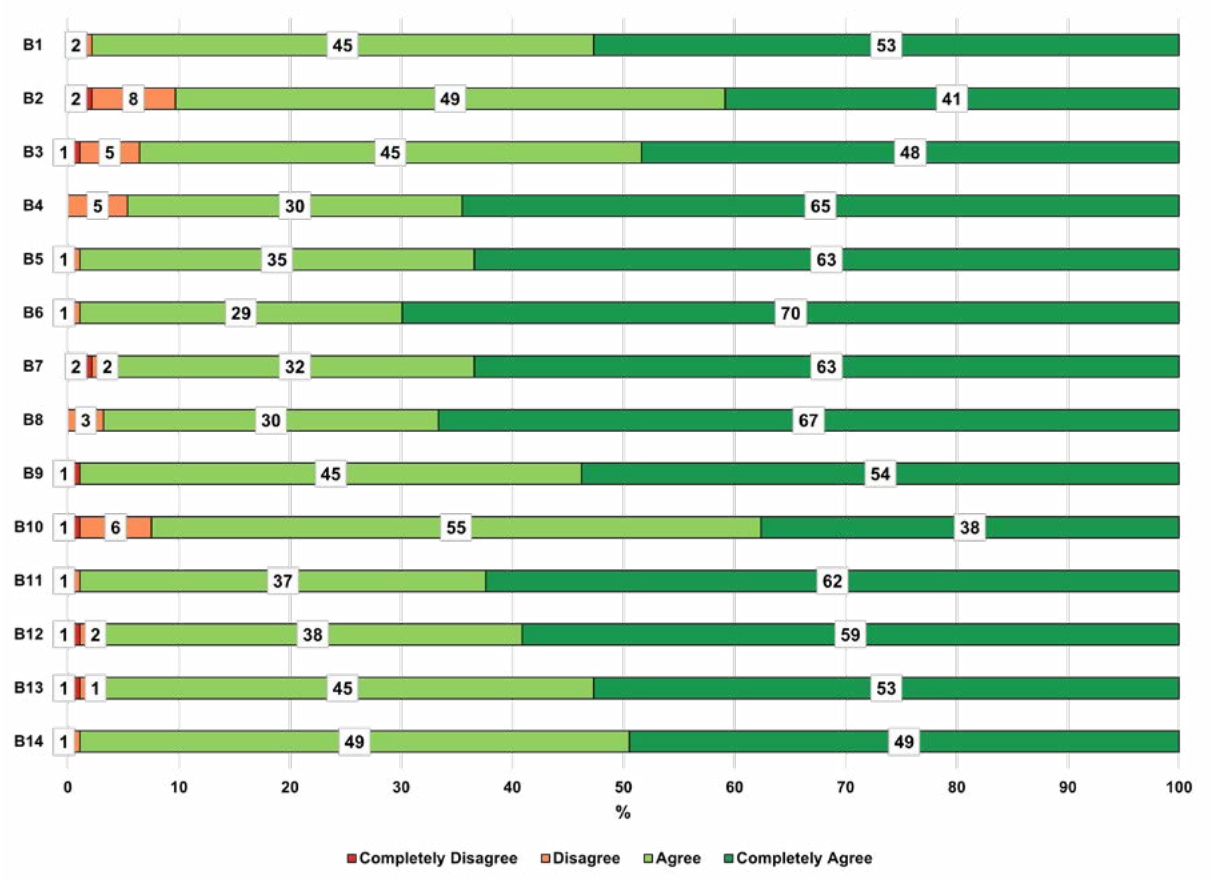

Figure 3. Overall characterization of statements (per %) from domain B – Clinical practice and therapeutic strategies.

Domain C: Availability and Access to K^+ Binders

This domain showed the highest overall endorsement, with majority agreement ranging from 96% to 100%. Statements C1 and C2 both achieved formal consensus (Fig. 4).

Statement C1, recommending hospital dispensing systems that ensure continuity of maintenance therapy between outpatient visits, achieved 100% majority agreement. Statement C2, identifying case-by-case Pharmacy and Therapeutics Committee approval as a barrier to therapeutic optimization and advocating streamlined institutional processes, also reached formal consensus (Fig. 4).

Dispensing by hospital pharmacists with counselling on administration, adverse effects, and precautions (Statement C3) achieved 100% majority agreement. Inclusion of new K^+ binders within community proximity-dispensing frameworks (Statement C4) and recognition of community pharmacies as key partners in medication reconciliation and maintenance of hospital-prescribed RAASi therapy (Statement C5) achieved 97% and 96%, respectively (Fig. 4).

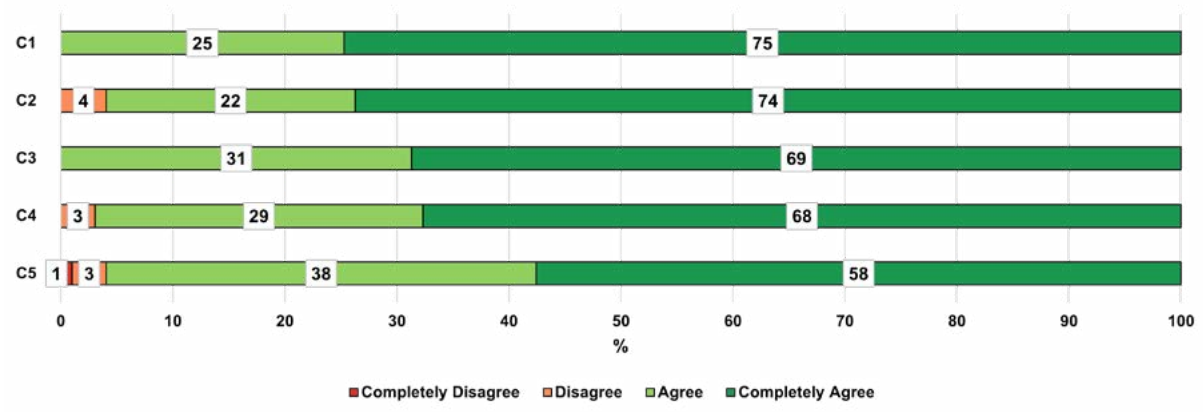

Figure 4. Overall characterization of statements (per %) from domain C – Availability and access to new K+ binders.

Table S2. Expert Delphi panel findings on clinical practice and therapeutic strategies (consensus and agreement levels).

B. CLINICAL PRACTICE AND THERAPEUTIC STRATEGIES	CA	IM	NE	ALL
1. Patients with CKD and/or cardiovascular-kidney-metabolic syndrome should be considered at risk for hyperkalemia based on an integrated clinical assessment, including: a. CKD severity: estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m² and urinary albumin-to-creatinine ratio (UACR) >300 mg/g b. Prior history of hyperkalemia c. Diagnosis of diabetes mellitus d. Diagnosis of heart failure (HF) e. Treatment with renin–angiotensin–aldosterone system inhibitors (RAASi) f. Baseline serum K^+ levels >4.5 mmol/L	M (100%)	M (97%)	M (97%)	M (98%)
2. In acute hyperkalemia associated with acute kidney injury, assessment of kidney function should not rely on estimated GFR, given the limitations of this parameter in non–steady-state conditions.	M (96%)	M (87%)	M (90%)	M (90%)
3. Chronic hyperkalemia is recommended to be defined as persistent serum K^+ ≥5.1 mmol/L in ≥2 laboratory assessments over ≥4 weeks (after excluding pseudohyperkalemia). Hyperkalemia should be classified as: Mild (serum K^+ 5.1–5.9 mmol/L without ECG changes); Moderate (serum K^+ 5.1–5.9 mmol/L with ECG changes, or serum K^+ 6.0–6.4 mmol/L without ECG changes); or Severe (serum K^+ 6.0–6.4 mmol/L with ECG changes, or serum K^+ ≥6.5 mmol/L without ECG changes)	M (88%)	M (95%)	M (97%)	M (94%)
4. Reduction or discontinuation of guideline-directed medical therapies in patients with CKD and/or HF due to hyperkalemia should be avoided whenever effective alternatives are available.	M (88%)	C	M (97%)	M (95%)
5. Management of hyperkalemia should be proactive, with regular laboratory monitoring of serum K^+ in patients receiving potentially hyperkalemia-inducing therapies, particularly RAAS inhibitors.	M (100%)	M (97%)	C	M (99%)
6. The use of new K+ binders in acute hyperkalemia may reduce the need for renal replacement therapy and should be incorporated into hospital protocols.	M (96%)	C	C	C
7. The use of new K+ binders is clinically appropriate in the chronic management of hyperkalemia, when required to allow continuation of RAAS inhibitor therapy.	M (88%)	C	C	M (96%)
8. New K+ binders should be preferred over traditional resins, due to their superior efficacy, tolerability, and safety profile.	M (100%)	M (97%)	C	M (97%)
9. The choice between patiromer and sodium zirconium cyclosilicate should consider mechanism of action, safety and tolerability profile, time to achieve normokalemia, risk of hypomagnesemia, drug–drug interactions and storage requirements	M (100%)	M (97%)	M (100%)	M (99%)
10. Patiromer may be considered for the treatment of hyperkalemia in the chronic maintenance setting, based on currently approved indications.	M (88%)	M (89%)	M (100%)	M (92%)
11. Sodium zirconium cyclosilicate may be considered for the treatment of hyperkalemia in acute correction and/or chronic maintenance, based on currently approved indications.	M (96%)	C	C	M (99%)
12. Based on recent scientific evidence, sodium zirconium cyclosilicate should be considered for the chronic treatment of hyperkalemia in adult patients with CKD stages 3–5, including patients with end-stage kidney disease or those enrolled in a regular hemodialysis program.	M (96%)	M (97%)	C	M (97%)
13. In patients treated with sodium zirconium cyclosilicate who have pre-existing heart failure, particularly those in whom increased sodium intake may lead to fluid overload and decompensation, monitoring for signs of HF worsening is recommended and management should follow standard clinical practice.	M (100%)	M (97%)	M (97%)	M (98%)
14. In patients treated with patiromer, serum Mg2+ levels should be monitored regularly, and cases of hypomagnesemia should be treated with appropriate supplementation.	M (100%)	M (100%)	M (97%)	M (99%)

CA, cardiology; IM, internal medicine; NE, nephrology; C, consensus agreement ("completely agree" ≥70%); M, majority agreement ("agree" + "completely agree" ≥70%)
In light green, the statements where majority was obtained among all experts (≥70% of "completely agree" + "agree"); in dark green, the statements where consensus was identified (≥70% of "completely agree")

Table S3. Expert Delphi panel findings on availability and access to new potassium (K+) binders (consensus and agreement levels)

C. AVAILABILITY AND ACCESS TO NEW K+ BINDERS	CA	IM	NE	PH	ALL
1. Hospital dispensing of new K^+ binders should ensure continuity of maintenance therapy between outpatient visits, avoiding treatment interruptions and unnecessary travel to the hospital pharmacy	M (100%)	C	C	M (100%)	C
2. The requirement for case-by-case approval by the Pharmacy and Therapeutics Committee (P&T Committee) for prescribing new K^+ binders represents a barrier to therapeutic optimization. This process should be simplified and supported by hospital dispensing protocols, avoiding delays in treatment initiation for eligible patients.	M (96%)	C	C	M (100%)	C
3. Whenever possible, on the day of the consultation, the hospital pharmacist should dispense the prescribed K^+ binder and instruct the patient on administration, potential adverse effects, and relevant precautions.	M (100%)	M (100%)	C	C	M (100%)
4. According to Order No. 10110/2024 of August 29, community-based dispensing (proximity dispensing) should consider new K^+ binders as a strategy for the treatment of hyperkalemia, in order to improve adherence to guideline-directed medical therapies and reduce the risk of morbidity and mortality in patients with CKD and/or cardiorenometabolic syndrome.	M (92%)	C	C	M (100%)	M (97%)
5. Within the proximity dispensing framework, community pharmacies will play a crucial role in medication reconciliation and in maintaining RAAS inhibitor therapy prescribed by the hospital treating physician.	M (92%)	M (95%)	C	M (100%)	M (96%)

CA, cardiology; IM, internal medicine; NE, nephrology; PH, pharmacy; C, consensus agreement ("completely agree" ≥70%); M, majority agreement ("agree" + "completely agree" ≥70%).
In light green, the statements where majority was obtained among all experts (≥70% of "completely agree" + "agree"); in dark green, the statements where consensus was identified (≥70% of "completely agree").

Subgroup Analysis

Although overall agreement was high across all specialties, some differences were observed. Nephrologists tend to express stronger levels of agreement. Pharmacists showed strong alignment in areas related to access and medication management. No statements reached formal consensus among cardiologists in any of the domains (Supplementary Figs. S1-S3).

In domain A, formal consensus was reached in three out of nine statements among nephrologists and in two out of nine among internists (Supplementary Fig. S1).

In domain B, consensus was achieved in six out of fourteen statements among nephrologists and in four out of fourteen among internists (Supplementary Fig. S2).

In domain C, formal consensus was reached for all statements among nephrologists (five out of five) and in three out of five statements among internists. One statement reached formal consensus among pharmacists (Supplementary Fig. S3).

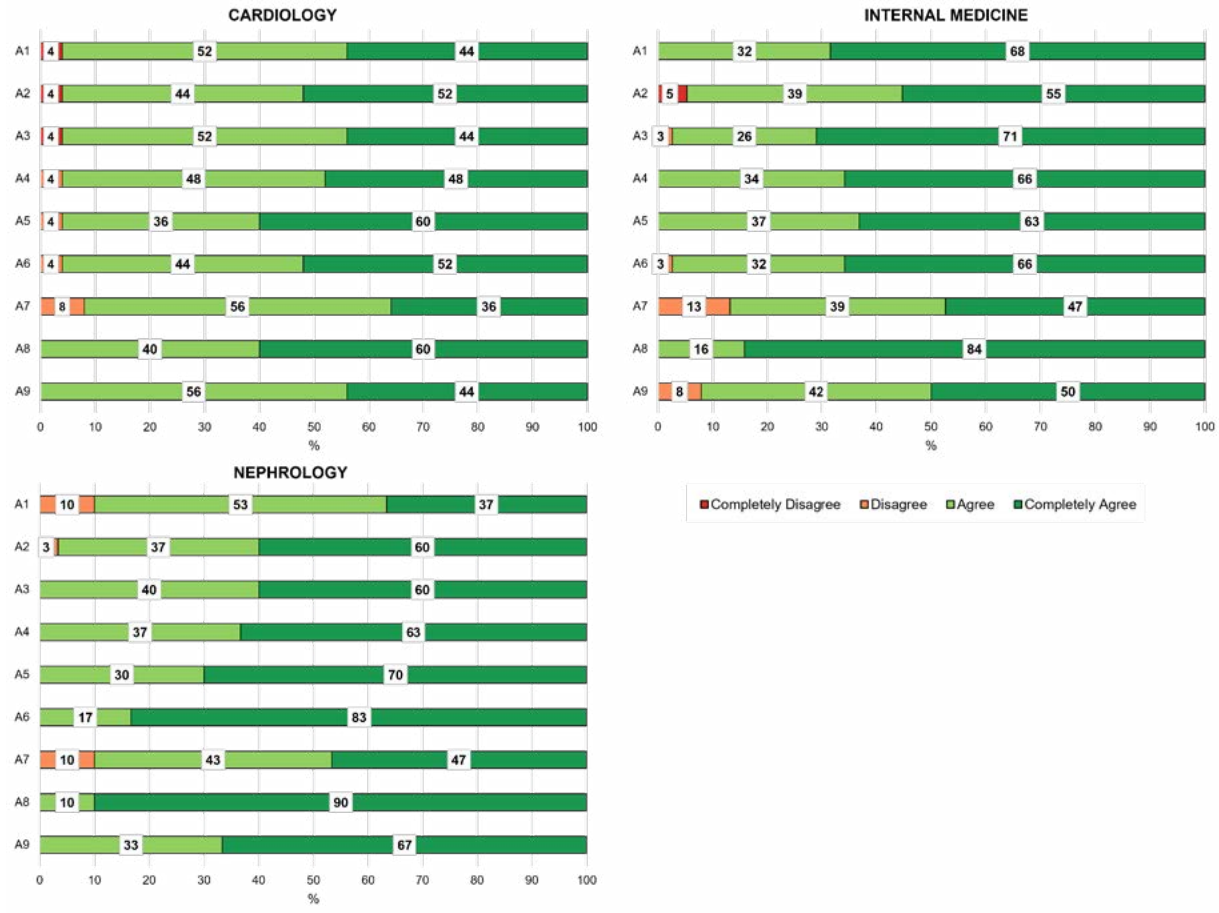

Figure S1. Characterization of statements (per %) from domain A – Healthcare organization and care pathways, according to medical specialty: cardiology, internal medicine and nephrology

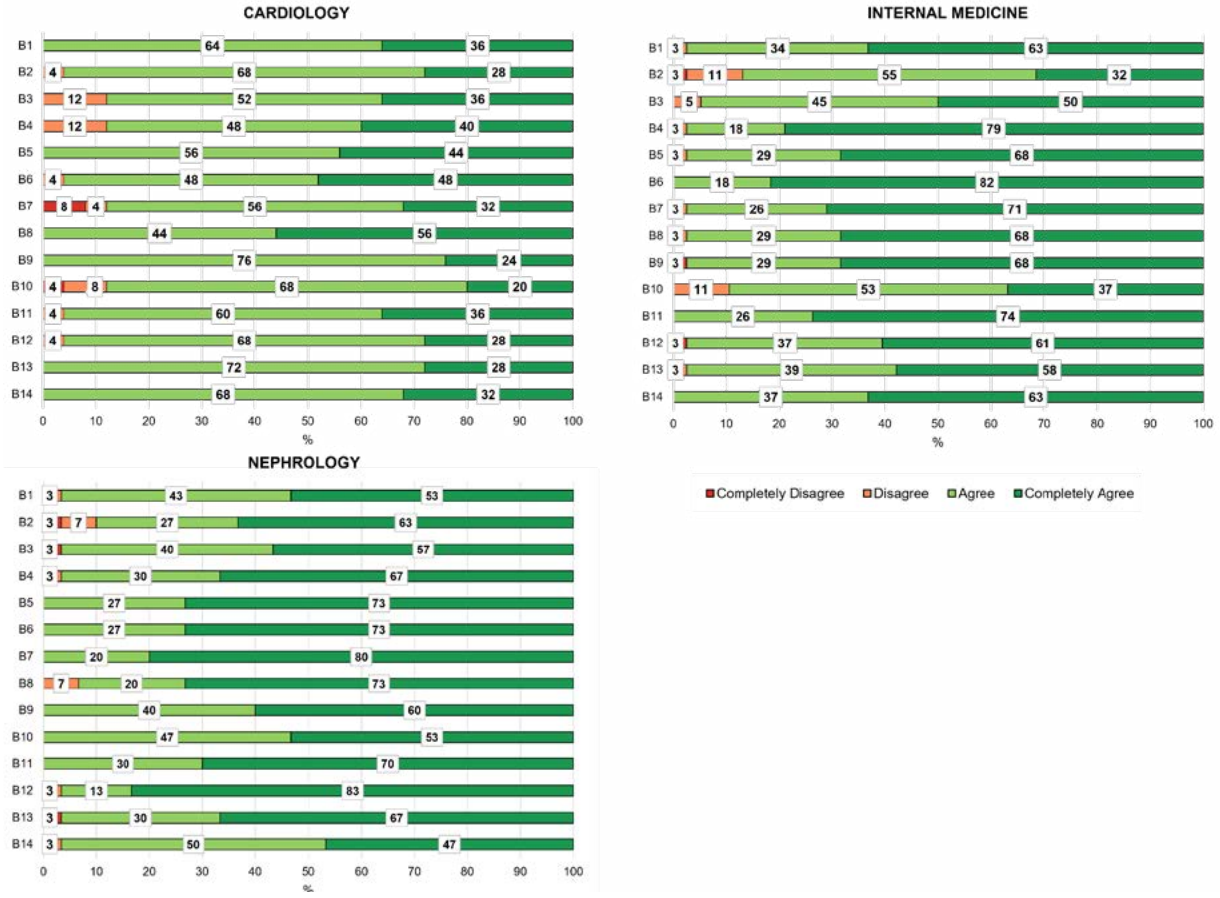

Figure S2. Characterization of statements (per %) from domain B – Clinical practice and therapeutic strategies, according to medical specialty: cardiology, internal medicine and nephrology.

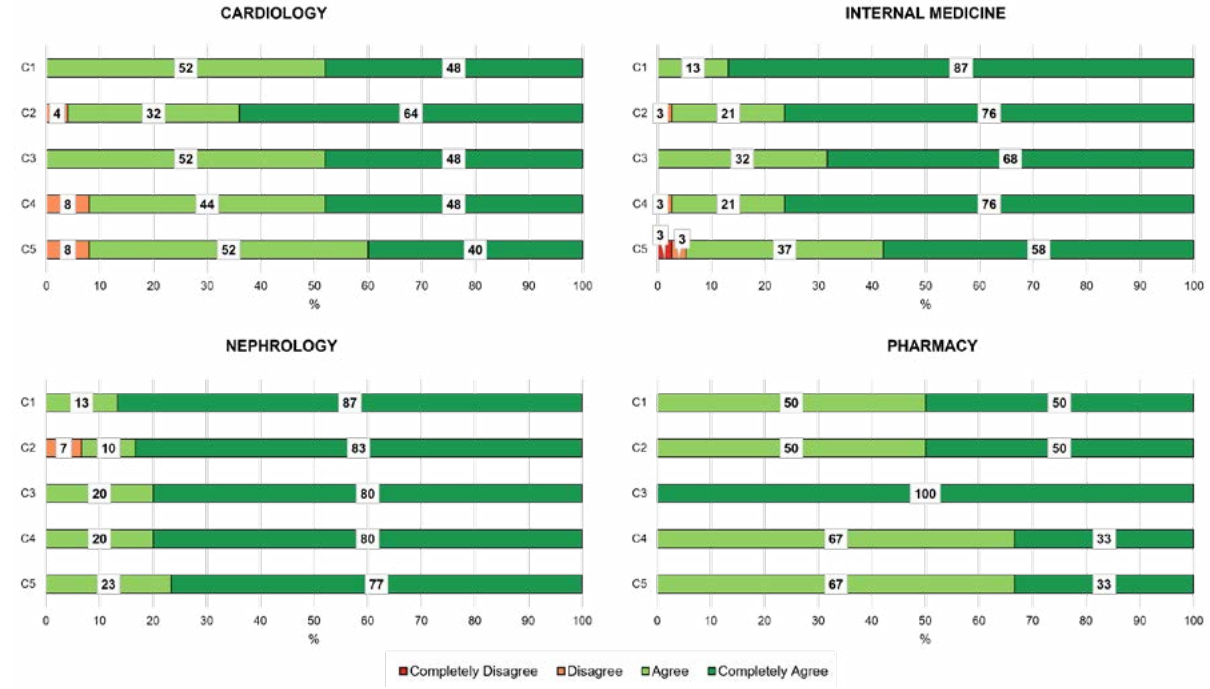

Figure S3. Characterization of statements (per %) from domain C – Availability and access to new K+ binders, according to healthcare specialty: cardiology, internal medicine, nephrology and pharmacy.

DISCUSSION

The present Delphi initiative provides a nationwide perspective on how HK is currently managed in Portugal and, importantly, identifies several areas of improvement. Across all domains, there were consistently high levels of agreement, suggesting that the proposed measures are not only theoretically appropriate but also recognized as feasible within national routine clinical practice. These findings are aligned with previous Portuguese consensus recommendations on HK management in the emergency setting, which emphasized both acute treatment and the prevention of recurrence.[16] Taken together, the present results support a transition from acute and episodic management of HK to more proactive and coordinated approaches that focus on prevention and sustained chronic management.

In terms of healthcare organization, several elements emerged as particularly relevant. There was robust support for defining K^+ thresholds that refer to specific clinical actions (Statement A2), indicating a need to reduce uncertainty in routine practice and decision-making. A known remaining issue in HK management is the lack of standardization in the timing for intervention or referral of patients.[17] Accordingly, the development of unified protocols adapted to the reality of each healthcare institution is seen as an advantage. Closely related to this, the implementation of structured pathways across care settings (Statement A3) reflects the reality that patients with HK often transition across emergency, inpatient, and outpatient care settings. Without clearly defined transitions, opportunities for timely and integrated intervention may be lost.[18]

The importance of early reassessment (Statement A5) further reinforces the idea that HK should not be viewed as a single event, but rather as a condition requiring periodic monitoring and continuous management.[17,19] Mechanisms such as follow-up visits, open-access clinics or day care hospital evaluation may help detect persistent or recurrent variations before they translate into preventable clinical decompensation and acute events. This perspective is consistent with recent recommendations from the GUARDIAN-HK European Steering Committee, which advocates a preventive and comprehensive strategy during acute HK episodes to improve both short- and long-term outcomes.[7]

The panel also strongly supported multidisciplinary collaboration (Statement A6), reflecting the complex clinical profile of patients at risk of HK, who often present with overlapping cardiovascular, renal, and metabolic diseases.[18,20] Coordinated management between cardiology, nephrology and internal medicine departments may facilitate individualized adjustment of GDMT while minimizing treatment-related risks, particularly unnecessary discontinuation or down-titration of RAASi. Furthermore, integrated laboratory surveillance systems across the entire healthcare network, including both hospital and primary care settings, could represent an additional strategy to improve early detection and management of HK. Automated alerts triggered by elevated K^+ values, regardless of the clinical setting in which they are identified, could facilitate timely medical review and intervention, potentially reducing delays in treatment and preventing progression to severe HK.

Patient involvement in the management of HK was also considered essential. The consensus regarding patient education (Statement A8) highlights that effective HK management extends beyond the clinical setting. Improving patient awareness of dietary factors, warning signs, and medication-related risks may contribute to earlier detection and better adherence to therapeutic strategies.[21]

In terms of clinical practice, the panel emphasized a comprehensive approach to CKM syndrome risk assessment (Statement B1), integrating renal function, comorbidities, prior history of HK episodes, and concomitant therapies. This approach reflects the current thinking that HK risk is multifactorial and should be contemplated within an integrated clinical assessment.[17] In this context, maintaining GDMT (Statement B4) emerged as particularly important. Previously, HK has often led to dose reduction or discontinuation of medications such as RAASi therapy.[8,9,22] Against this background, new K^+ binders have emerged as an important strategy for active K^+ management, particularly when the goal is to maintain or optimize RAASi therapy.[8,10,23,24] These findings indicate increasing use of active K^+ management to maintain normokalemia and enable RAASi therapy, thereby preserving long-term cardiovascular and renal benefits of this class.

In acute HK, the consensus agreement on the inclusion of these agents in acute treatment protocols (Statement B6) suggests growing confidence among clinicians in their ability to complement existing strategies and potentially reduce the need for more invasive interventions, such as dialysis.[25]

In chronic HK, support for the use of these agents to facilitate the maintenance and optimization of RAASi therapy (Statement B7) reflects an approach aimed at improving long-term cardiovascular and renal outcomes,[9] given that RAASi constitutes a fundamental pharmacological pillar in the management of patients with CKD and HF. This is supported by randomized controlled trials demonstrating effective K^+ control and enabling continuation of RAASi therapy, including OPAL-HK, HARMONIZE, REALIZE-K, and DIAMOND, although these studies were not powered to assess long-term cardiovascular or renal outcomes.[27-30]

Real-world evidence supports the use of long-term K^+ binders to enable optimization and maintenance of guideline-directed RAASi therapy in patients with HK, as demonstrated in an international cohort study, where treatment with zirconium was associated with a higher likelihood of maintained RAASi therapy after a HK episode.[26]

Real-world evidence further supports improved RAASi persistence and reduced treatment discontinuation associated with K^+ binder use in routine clinical practice. Namely, findings from the GALVANIZE study suggested that zirconium supported the maintenance of optimal RAASi therapy in patients with CKD and HF.[31] In addition, in a propensity-matched real-world population (Salford Kidney Study) with the AMETHYST-DN trial, the benefit of patiromer for HK management to enable RAASi was demonstrated.[32]

In this line, the impact on healthcare resource utilization has also been noted. The GALVANIZE Outcome and the VITALIZE studies showed that sustained treatment with zirconium was associated with a reduction in HK-related healthcare encounters, supporting longer-term K^+ control strategies in patients with HF and cardiorenal dysfunction.[33,34] Similarly, findings from the VALUE study demonstrated that longer-term use of patiromer was associated with lower healthcare resource utilization compared with short-term treatment.[35] Altogether, these studies further support the role of sustained K^+-lowering therapy in the long-term management of patients at risk of recurrent HK, as well as reductions in HK-related hospitalizations and emergency department visits. Also, the overall agreement that newer binders are preferable over traditional resins (Statement B8) likely relates to their improved tolerability, efficacy and more predictable pharmacological profiles.[36]

At the same time, the panel acknowledged that treatment selection should follow an individualized approach, taking into account factors such as onset of action, safety profile, and potential drug interactions (Statement B9). The differentiated roles proposed for patiromer (chronic setting) and zirconium (acute and chronic settings) (Statements B10–B11) are consistent with their pharmacological characteristics and the available evidence,[36] including in patients with advanced CKD (Statement B12).[28,37]

Safety monitoring was also emphasized. In patients receiving patiromer, Mg^{2+} levels should be regularly monitored (Statement B14) because of the drug's binding to Mg^{2+} in the colon and the associated risk of hypomagnesemia.[38] In addition, clinicians should be aware of potential drug–drug interactions with patiromer (Statement B9). Patiromer can bind to several commonly prescribed oral medications in patients with CKM syndrome, including metformin, ciprofloxacin, telmisartan, and bisoprolol, potentially reducing their gastrointestinal absorption. Therefore, administration of these medications should be separated from patiromer by at least 3 hours.[38] Given the high prevalence of diabetes, hypertension, and cardiovascular disease in this population, attention to dosing schedules is particularly important to ensure therapeutic efficacy.

By contrast, the effects of zirconium on the absorption of concomitant medications appear to be limited, and dose adjustments or administration time separation are generally not required. Zirconium may be administered concomitantly with oral medications that do not exhibit pH-dependent bioavailability.[39] Only for drugs with pH-dependent absorption is a dosing interval of at least 2 hours recommended; examples include azole antifungals, certain antiretroviral agents, and tyrosine kinase inhibitors, which are less commonly used in patients with CKM syndrome.[39] Likewise, patients receiving zirconium, particularly those with pre-existing HF, should be monitored according to standard clinical practice for signs and symptoms of fluid overload or worsening HF, including rapid weight gain, edema, or increased dyspnea.[39]

Beyond clinical efficacy and safety, treatment decisions should also incorporate patient preferences and shared decision-making between clinicians and patients, even though these aspects were not specifically captured in the Delphi statements. Factors such as palatability and ease of administration may influence treatment acceptance and adherence.[40] The APPETIZE study showed that zirconium and patiromer outperformed sodium and calcium polystyrene sulfonate (S/CPS) on overall palatability, and that greater proportion of participants ranked zirconium as the most preferred K^+ binder versus patiromer or S/CPS.[40] Additionally, maintaining a consistent therapeutic strategy across inpatient and outpatient settings, as determined by the treating physician, may contribute to improved treatment adherence and continuity of care, particularly given the role of zirconium in both acute and chronic HK management.[41]

Issues related to availability and access to new K^+ binders were among those with the highest levels of agreement. Ensuring therapy maintenance through hospital dispensing (Statement C1) was viewed as essential to avoid treatment interruptions that could lead to HK recurrence.[17,42] At the same time, administrative requirements, such as case-by-case approval processes (Statement C2), were consensually identified as barriers to timely treatment initiation. Simplification of these pathways and implementation of standardized dispensing protocols may facilitate the translation of clinical decisions into practice.

The role of pharmacists was also recognized by the panel as increasingly relevant. Dispensing on the same day of the consultation, together with patient counselling regarding administration, adverse effects and precautions (Statement C3), may improve both adherence and correct use of therapy. The panel agreed, particularly internists and nephrologists, in the inclusion of new K^+ binders proximity dispensing schemes established under Order No. 10110/2024 of August 29, 2024 (Statement C4).[43] These findings are consistent with efforts to decentralize healthcare delivery and strengthen the interface between hospital- and community-based care.

Overall, the findings indicate that meaningful improvements in HK management in Portugal are likely to be achieved through better alignment between care pathways, therapeutic decision-making, and access to treatment.

Several limitations of this study should be considered. The Delphi methodology reflects expert opinion and should not be interpreted as evidence of comparative effectiveness. Despite having reached high agreement rates (≥89%), the study included only one survey round, which may have reduced the opportunity to further refine areas of partial agreement. Although the multidisciplinary Delphi panel included specialists from nephrology, cardiology, internal medicine and hospital pharmacy, the steering group responsible for statement development had a greater representation of nephrologists. This may have influenced the framing and prioritization of some recommendations despite the high level of agreement achieved across specialties. The relatively small number of pharmacists also limited the breadth of input on medication management and access-related issues. Also, although high levels of agreement were observed and the recommendations had been extensively discussed during the face-to-face multidisciplinary meetings preceding the Delphi exercise, this study was limited to a single voting round. Consequently, the stability of participants' responses over time could not be formally assessed. Finally, some recommendations have the underlying organizational and regulatory characteristics of the Portuguese healthcare system, which limit generalizability to other settings without appropriate adaptation. Nonetheless, the consistently high levels of agreement across statements support the robustness of the conclusions and suggest broad recognition of current gaps and priorities in HK management.

In conclusion, these findings underscore the need for a more proactive, integrated approach to HK management in Portugal, with particular emphasis on early identification, sustained use of GDMT, appropriate incorporation of newer pharmacological options, and reduction of barriers to treatment access (Fig. 5).

Future studies should assess the real-world implementation of these practical recommendations and determine whether their adoption translates into measurable improvements in patient outcomes.

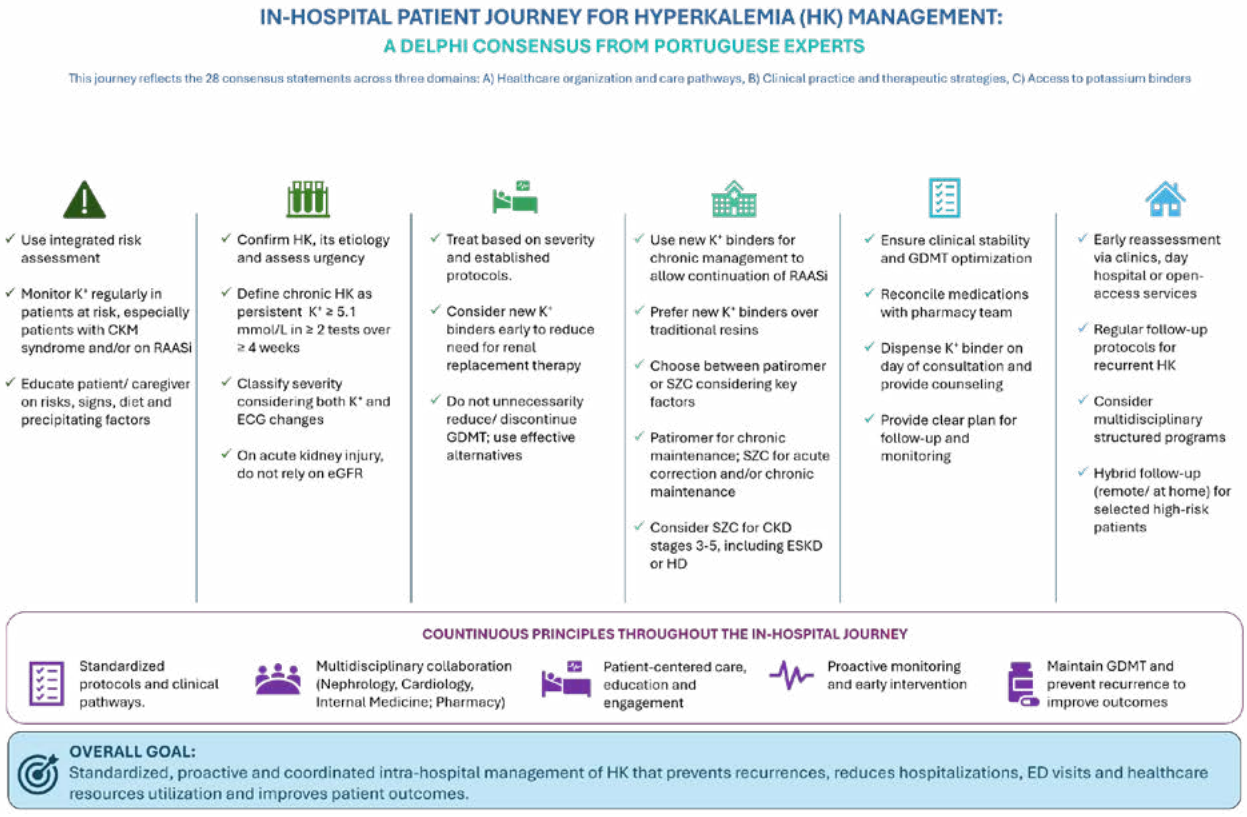

Figure 5. In-hospital patient journey for hyperkalemia management. This figure reflects the 28 statements that reached a majority of agreement among experts, proposing an optimized intra-hospital patient journey regarding hyperkalemia management

Abbreviations: CKD, chronic kidney disease; CKM, cardiovascular-kidney-metabolic; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; ED, emergency department; ESKD, end-stage kidney disease; GDMT, guideline-directed medical therapy; HD, hemodialysis; HF, heart failure; HK, hyperkalemia; K^+, potassium; Mg^{2+}, magnesium; RAASi, renin-angiotensin-aldosterone system inhibitor; SZC, sodium zirconium cyclosilicate.

Acknowledgements
The authors would like to acknowledge the healthcare professionals that participated in the multidisciplinary roundtables (Ana Castro, António Gonçalves, António Pedro Gonçalves, Bruno Sousa, Carla Rafaela Ferreira, Carolina Negrier, Catarina Gomes, Cristina Marujo, Diogo Borges, Eunice Loureiro, Filipa Gomes, Isabel Chaves, Joana Nascimento, Jorge Mimoso, José Mariz, Luís Mendonça, Otília Simões, Pedro Carreira, Rui Domingues, Tatiana Duarte, Vera Batista, Vitor Braz), to AstraZeneca for organizational support (Ana Catarina Gomes, Daniel Ramos, João Couceiro, Marcos Correia, Rita Canhoto, Rolanda Pacheco, Rudolfo Francisco) and medical writing support provided by Evidenze Portugal. The funder did not influence expert opinions, data interpretation and conclusions.

Authors Contributions
All authors made a significant contribution to the work reported, including conception, design, execution, acquisition of data, analysis and interpretation; drafting and reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Conflict of Interest and Sources of Funding Statement
This work was funded by AstraZeneca. The sponsor provided financial and logistical support for the project but had no role in the roundtable moderation, discussion and development of the consensus statements, voting process, interpretation of results, or formulation of the recommendations. Support for study conduct and medical writing was provided by Evidenze Portugal.

The authors declare the following competing interests:
- Ana Natário has received speaker fees from Fresenius Kabi, AstraZeneca, Boehringer Ingelheim, Bayer, and Dietcare.
- Irene Marques has received speaker and consultancy fees from AstraZeneca, Bayer, Bial, CSL Vifor, Daiichi Sankyo, Eli Lilly, Novartis, Novo Nordisk, Pfizer, Roche Diagnostics, and Servier. IM also serves as coordinator of the Núcleo de Estudo de Insuficiência Cardíaca of the Portuguese Society of Internal Medicine.
- Marco Mendes has received speaker and consultancy fees from AstraZeneca and CSL Vifor.
- João Porto has received speaker and consultancy fees from AstraZeneca and Tecnifar, as well as support for attending meetings from Tecnifar, Viatris, and Servier. JP holds positions within the Portuguese Society of Internal Medicine, the Portuguese Society of Atherosclerosis, and the Portuguese Medical Association
- Joana Paixão has received speaker fees from AstraZeneca.
- Rodrigo Leão has received speaker and consultancy fees from Novartis, Bayer, Jaba Recordati, Ferrer, and Menarini, and support for attending meetings from AstraZeneca, Tecnifar, and Daiichi Sankyo.
- Renata Carvalho has received support for attending meetings from Novartis and Fresenius Kabi, and speaker fees from AstraZeneca.
- Paulo Araújo has received speaker and consultancy fees from AstraZeneca, Amgen, and Novartis.
- Hugo Diniz has received royalties or licenses from PocusX; honoraria for lectures, presentations, or educational events from AstraZeneca, Eli Lilly, Boehringer Ingelheim, Bayer, CSL Vifor, and EchoNous; support for attending meetings and/or travel from AstraZeneca, Boehringer Ingelheim, and SonoScape; and has participated on an Advisory Board for Boehringer Ingelheim. Hugo Diniz also serves on the board of the Young Nephrologists' Platform of the European Renal Association (ERA).
- Cátia Oliveira, Ana Paula Silva, and Luís Rodrigues declare that they have no competing interests.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

REFERENCES
1. Hunter RW, Bailey MA. Hyperkalemia: pathophysiology, risk factors and consequences. Nephrol Dial Transplant. 2019;34:iii2-iii11. doi: 10.1093/ndt/gfz206.
2. Collins AJ, Pitt B, Reaven N, Funk S, McGaughey K, Wilson D, et al. Association of Serum Potassium with All-Cause Mortality in Patients with and without Heart Failure, Chronic Kidney Disease, and/or Diabetes. Am J Nephrol. 2017;46:213-21. doi: 10.1159/000479802.
3. Sharma A, Alvarez PJ, Woods SD, Fogli J, Dai D. Healthcare resource utilization and costs associated with hyperkalemia in a large managed care population. J Pharm Health Serv Res. 2021;12:35-41. doi: 10.1093/jphsr/rmaa004.

4. Joo JY. Fragmented care and chronic illness patient outcomes: A systematic review. Nurs Open. 2023;10:3460-73.
5. Ndumele CE, Rangaswami J, Chow SL, Neeland IJ, Tuttle KR, et al; American Heart Association. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. Circulation. 2023;148:1606-35. doi: 10.1161/CIR.0000000000001184. Epub 2023 Oct 9. Erratum in: Circulation. 2024;149:e1023. doi: 10.1161/CIR.0000000000001241
6. Fujimaru T, Hirose K, Yazawa M, Nagahama M, Kovesdy CP; Electrolyte Winter Seminar Collaborative Group. Management of hyperkalemia: strategic clinical actions in real-world practice. Clin Exp Nephrol. 2025;29:1699-711. doi: 10.1007/s10157-025-02728-2.
7. Savarese G, Izquierdo MJ, Bonanad C, Wong A, Schmitt R, Ferraro PM, et al. Interdisciplinary recommendations for recurrent hyperkalaemia: insights from the GUARDIAN-HK European Steering Committee. Eur Heart J Cardiovasc Pharmacother. 2025;11:630-7. doi: 10.1093/ehjcvp/pvaf055.
8. Fonseca C, Garagarza C, Silva G, Caires G, Marques I, Lopes JA, et al. Hyperkalemia management: a multidisciplinary expert panel's perspective on the role of new potassium binders. Heart Fail Rev. 2025;30:271-86. doi: 10.1007/s10741-024-10461-3.
9. Silva-Cardoso J, Brito D, Frazão JM, Ferreira A, Bettencourt P, Branco P, Fonseca C. Management of RAASi-associated hyperkalemia in patients with cardiovascular disease. Heart Fail Rev. 2021;26:891-6. doi: 10.1007/s10741-020-10069-3.
10. Huang N, Xu Y, Liu C, Liu Y, Fan Y, Li Z, et al. Novel Potassium binders in reduction of hyperkalemia and optimization of RAAS inhibitors treatment in patients with chronic kidney disease or heart failure: a systematic review and meta-analysis. Drugs. 2025;85:1013-31. doi: 10.1007/s40265-025-02198-6.
11. Rosano GM, Tamargo J, Kjeldsen KP, Lainscak M, Agewall S, Anker SD, et al. Expert consensus document on the management of hyperkalaemia in patients with cardiovascular disease treated with renin angiotensin aldosterone system inhibitors: coordinated by the Working Group on Cardiovascular Pharmacotherapy of the European Society of Cardiology. Eur Heart J Cardiovasc Pharmacother. 2018;4:180-8. doi: 10.1093/ehjcvp/pvy015.
12. Alfonzo A, Harrison A, Baines R, Chu A, Mann S, MacRury M. UKKA clinical practice guideline: management of hyperkalaemia in adults. Bristol: UK Kidney Association; 2023 [cited 2025 June 18]. Available from: https://www.ukkidney.org/health-professionals/guidelines/treatment-acute-hyperkalaemia-adults-0
13. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105:S117-S314. doi: 10.1016/j.kint.2023.10.018.
14. National Institute for Health and Care Excellence (NICE). Chronic heart failure in adults: diagnosis and management. London: NICE; 2018.
15. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022;79:1757-80. doi: 10.1016/j.jacc.2021.12.011.
16. Sá Sousa A, da Luz Brazão M, Marujo C, Fortuna I, Almeida I, Almeida JL, et al. Management of Hyperkalemia in an Emergency Situation: Best Practices Recommendations Driven by Consensus Methodology: Gestão da Hipercalemia em Contexto de Urgência: Recomendações de Boas Práticas Geradas por Metodologia de Consenso. Rev Port Med Interna. 2024;31:132-41.
17. Ortiz-Cortés C, Navarro-González JF; advisory board of the Instituto de Hiperkalemia IHK. Current insights and challenges in the management of hyperkalemia. Rev Esp Cardiol. 2026;79:369-76. doi: 10.1016/j.rec.2025.10.012.
18. Kreitzer N, Albert NM, Amin AN, Beavers CJ, Becker RC, Fonarow G, et al. EMCREG-International Multidisciplinary Consensus Panel on Management of Hyperkalemia in Chronic Kidney Disease and Heart Failure. Cardiorenal Med. 2025;15:133-52. doi: 10.1159/000543385.
19. Ortiz A, Galán CD, Carlos Fernández-García J, Cerezo JG, Ochoa RI, Núñez J, et al. Consensus document on the management of hyperkalemia. Nefrologia. 2023;43:765-82. doi: 10.1016/j.nefroe.2023.12.002.
20. Dunn JD, Benton WW, Orozco-Torrentera E, Adamson RT. The burden of hyperkalemia in patients with cardiovascular and renal disease. Am J Manag Care. 2015;21:s307-15.
21. Palmer BF, Carrero JJ, Clegg DJ, Colbert GB, Emmett M, Fishbane S, et al. Clinical Management of Hyperkalemia. Mayo Clin Proc. 2021;96:744-62. doi: 10.1016/j.mayocp.2020.06.014.
22. Fonseca C, Brito D, Branco P, Frazão JM, Silva-Cardoso J, Bettencourt P. Hyperkalemia and management of renin-angiotensin-aldosterone system inhibitors in chronic heart failure with reduced ejection fraction: A systematic review. Rev Port Cardiol. 2020;39:517-41. doi: 10.1016/j.repc.2020.03.015.
23. Wanner C, Zhao MH, Amin AN, De Nicola L, Sauer AJ, Allum AM, et al. Guideline-Recommended Disease-Modifying Therapies for Patients with Cardiorenal Disease: A Call-to-Action Narrative Review. Adv Ther. 2025;42:3141-57. doi: 10.1007/s12325-025-03228-1.
24. Peacock WF, Rafique Z, Gayle J, Neuenschwander J, Brown H, Kammerer J, et al. Outcomes and Resource Utilization in Hyperkalemic Emergency Department Patients Treated With Patiromer or Sodium Zirconium Cyclosilicate. J Am Coll Emerg Physicians Open. 2025;6:100158. doi: 10.1016/j.acepjo.2025.100158.
25. Masi S, Dalpiaz H, Piludu S, Piani F, Fiorini G, Borghi C. New strategies for the treatment of hyperkalemia. Eur J Intern Med. 2025;132:18-26. doi: 10.1016/j.ejim.2024.10.016.
26. Rastogi A, Pollack CV Jr, Sánchez Lázaro IJ, Lesén E, Arnold M, Franzén S, et al. Maintained renin-angiotensin-aldosterone system inhibitor therapy with sodium zirconium cyclosilicate following a hyperkalaemia episode: a multicountry cohort study. Clin Kidney J. 2024;17:sfae083. doi: 10.1093/ckj/sfae083.
27. Weir MR, Bakris GL, Bushinsky DA, Mayo MR, Garza D, et al; OPAL-HK Investigators. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. N Engl J Med. 2015;372:211-21. doi: 10.1056/NEJMoa1410853.
28. Kosiborod M, Rasmussen HS, Lavin P, Qunibi WY, Spinowitz B, Packham D, et al. Effect of sodium zirconium cyclosilicate on potassium lowering for 28 days among outpatients with hyperkalemia: the HARMONIZE randomized clinical trial. JAMA. 2014;312:2223-33. doi: 10.1001/jama.2014.15688.
29. Kosiborod MN, Cherney DZ, Desai AS, Testani JM, Verma S, Chinnakondepalli K, et al. Sodium Zirconium Cyclosilicate for Management of Hyperkalemia During Spironolactone Optimization in Patients With Heart Failure. J Am Coll Cardiol. 202585:971-84. doi: 10.1016/j.jacc.2024.11.014.
30. Butler J, Anker SD, Lund LH, Coats AJ, Filippatos G, Siddiqi TJ, et al. Patiromer for the management of hyperkalemia in heart failure with reduced ejection fraction: the DIAMOND trial. Eur Heart J. 2022;43:4362-373. doi: 10.1093/eurheartj/ehac401.

31. Agiro A, Greatsinger A, Mu F, Cook EE, Chen J, Sundar M, et al. Renin-Angiotensin-Aldosterone System Inhibitor Dosing After Initiation of Outpatient Sodium Zirconium Cyclosilicate Therapy: The GALVANIZE RAASi Real-World Evidence Study. Adv Ther. 2025;42:3960-77. doi: 10.1007/s12325-025-03254-z.
32. Chinnadurai R, Rengarajan S, Budden JJ, Quinn CM, Kalra PA. Maintaining Renin-Angiotensin-Aldosterone System Inhibitor Treatment with Patiromer in Hyperkalaemic Chronic Kidney Disease Patients: Comparison of a Propensity-Matched Real-World Population with AMETHYST-DN. Am J Nephrol. 2023;54:408-15. doi: 10.1159/000533753.
33. Agiro A, An A, Cook EE, Mu F, Chen J, Desai P, et al. Real-World Modifications of Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Hyperkalemia Initiating Sodium Zirconium Cyclosilicate Therapy: The OPTIMIZE I Study. Adv Ther. 2023;40:2886-901. doi: 10.1007/s12325-023-02518-w.
34. 5028-4. Utilización de recursos sanitarios en pacientes con hiperpotasemia antes y después del inicio de tratamiento con ciclosilicato de sodio y zirconio. Estudio VITALIZE [accessed Feb 2026] Available from: https://www.revespcardiol.org/es-congresos-sec-2025-el-congreso-de-la-salud-cardiov-178-sesion-5028-insuficiencia-cardiaca-de-la-basica-8794-comunicacion-utilizacion-de-recursos-sanitarios-en-pa-107658
35. Gupta A, Kammerer J, Shaik I, Mukherjee KG, Oliveira J, Thakar C. Evaluation of longer- vs short-term use of patiromer on health care resource utilization in the patiromer longer-term use evaluation (VALUE) study. J Manag Care Spec Pharm. 2024;30:52-60. doi: 10.18553/jmcp.2023.23100.
36. Zirino F, Maressa V, Messina RM, Stancanelli MR, Gembillo G, Longhitano E, et al. Differences in Efficacy Among New and Old Potassium Binders in Dialysis Patients: A Systematic Review and Meta-Analysis. G Ital Nefrol. 2025;42:2025-vol4. doi: 10.69097/42-04-2025-06.
37. National Institute for Health and Care Excellence (NICE), Technology appraisal guidance (TA599): Sodium zirconium cyclosilicate for treating hyperkalaemia. London: NICE; 2022.
38. Veltassa [summary of product characteristics]. 2018: Vifor Fresenius Medical Care Renal Pharma.
39. Lokelma [summary of product characteristics]. 2018: AstraZeneca AB.
40. Wheeler DC, Søndergaard H, Gwynn C, Hedman K, Hedberg J, Allum A, et al. Randomised, blinded, cross-over evaluation of the palatability of and preference for different potassium binders in participants with chronic hyperkalaemia in the USA, Canada and Europe: the APPETIZE study. BMJ Open. 2024;14:e074954. doi: 10.1136/bmjopen-2023-074954.
41. Religioni U, Barrios-Rodríguez R, Requena P, Borowska M, Ostrowski J. Enhancing Therapy Adherence: Impact on Clinical Outcomes, Healthcare Costs, and Patient Quality of Life. Medicina. 2025;61:153. doi: 10.3390/medicina61010153.
42. Rowan CG, Agiro A, Chan KA, Colman E, White K, Desai P, et al. Hyperkalemia Recurrence Following Medical Nutrition Therapy in Patients with Stage 3-4 Chronic Kidney Disease: The REVOLUTIONIZE I Real-World Study. Adv Ther. 2024;41:2381-98. doi: 10.1007/s12325-024-02835-8.
43. Gabinete da Secretária de Estado da Saúde. Despacho n.º 10110/2024, de 29 de agosto. 2024 [accessed Feb 2026] Available from: https://diariodarepublica.pt/dr/detalhe/despacho/10110-2024-886139756.