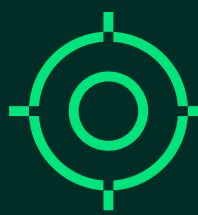


Understanding Physicians’ Decision-making Processes when Treating Mild-to-Moderate Chronic Kidney Disease: A Qualitative Study

James Fotheringham,¹ Keila Meginnis,² Matthew Quaife,² Anastasia Doldos,² John F. P. Bridges.³

1. School of Population Health, University of Sheffield, Sheffield, UK; 2. Evidera Ltd., a business unit of PPD, part of Thermo Fisher Scientific, London, UK; 3. The Ohio State University College of Medicine, Columbus, OH, USA.

Objectives



This qualitative preference study sought to understand mild-to-moderate chronic kidney disease (CKD) pharmacotherapy from a physician's perspective, with the objective of investigating (1) attitudes toward existing treatments and unmet needs, (2) the impact of patient characteristics on prescribing behaviors; and (3) how physicians weigh different risks and benefits when managing CKD.

Introduction



- Mild-to-moderate CKD is associated with increased risks of cardiovascular events, progression to end-stage renal disease, and overall mortality. CKD profoundly impacts public health because of its association with a range of complications, reduced quality of life, and increased healthcare costs.^{1,2} Underdiagnosis of early CKD exacerbates these issues.
- The broadening of the therapeutic landscape for mild-to-moderate CKD has come at a cost—renin-angiotensin-aldosterone system (RAAS) inhibitors and mineralocorticoid receptor antagonists (MRA) increase potassium levels, and sodium-glucose co-transporter-2 (SGLT2) inhibitors lower potassium levels.
- Decision-making for mild-to-moderate CKD treatment pathways can be complex, because physicians have to balance treatment benefits, such as slowing CKD progression, against treatment side effects.³
- Hyperkalemia is an important consideration in CKD management because CKD impairs the ability of the kidneys to regulate potassium levels,^{4,5} and also because various evidence-based, guideline-recommended drugs used to treat CKD increase potassium levels or reduce potassium excretion.⁶⁻⁸

Methods



- Eligible physicians were general practitioners, cardiologists, or nephrologists practicing in the US, UK, France, Germany or the Netherlands.
- Semistructured qualitative interviews took place between June and August 2023.
- The interview guide was developed using a targeted literature review of quantitative and qualitative physician perspective studies examining attitudes, behaviors, and preferences toward mild-to-moderate CKD treatments.
- Given the concern around hyperkalemia when treating patients with CKD, this study gathered qualitative and quantitative insights into the impact of hyperkalemia on decision-making.

Results



Sample characteristics

- Seventeen interviews were conducted with general practitioners (n=11; 65%), cardiologists (n=1; 6%), and nephrologists (n=5; 29%). Five interviews were conducted in the US, and three interviews were conducted in each of the other four countries.
- On average, physicians had 23 years of experience treating patients with mild-to-moderate CKD. Most worked in private practice (n=11; 65%), predominantly in urban areas or cities (n=9; 53%).
- In the past year, physicians saw an average 65.7 (SD: 80.8) patients at CKD stage 1, 78.9 (SD: 68.1) patients at CKD stage 2, 87.4 (SD: 67.7) patients at CKD stage 3a, and 76.4 (SD: 64.1) patients at CKD stage 3b.

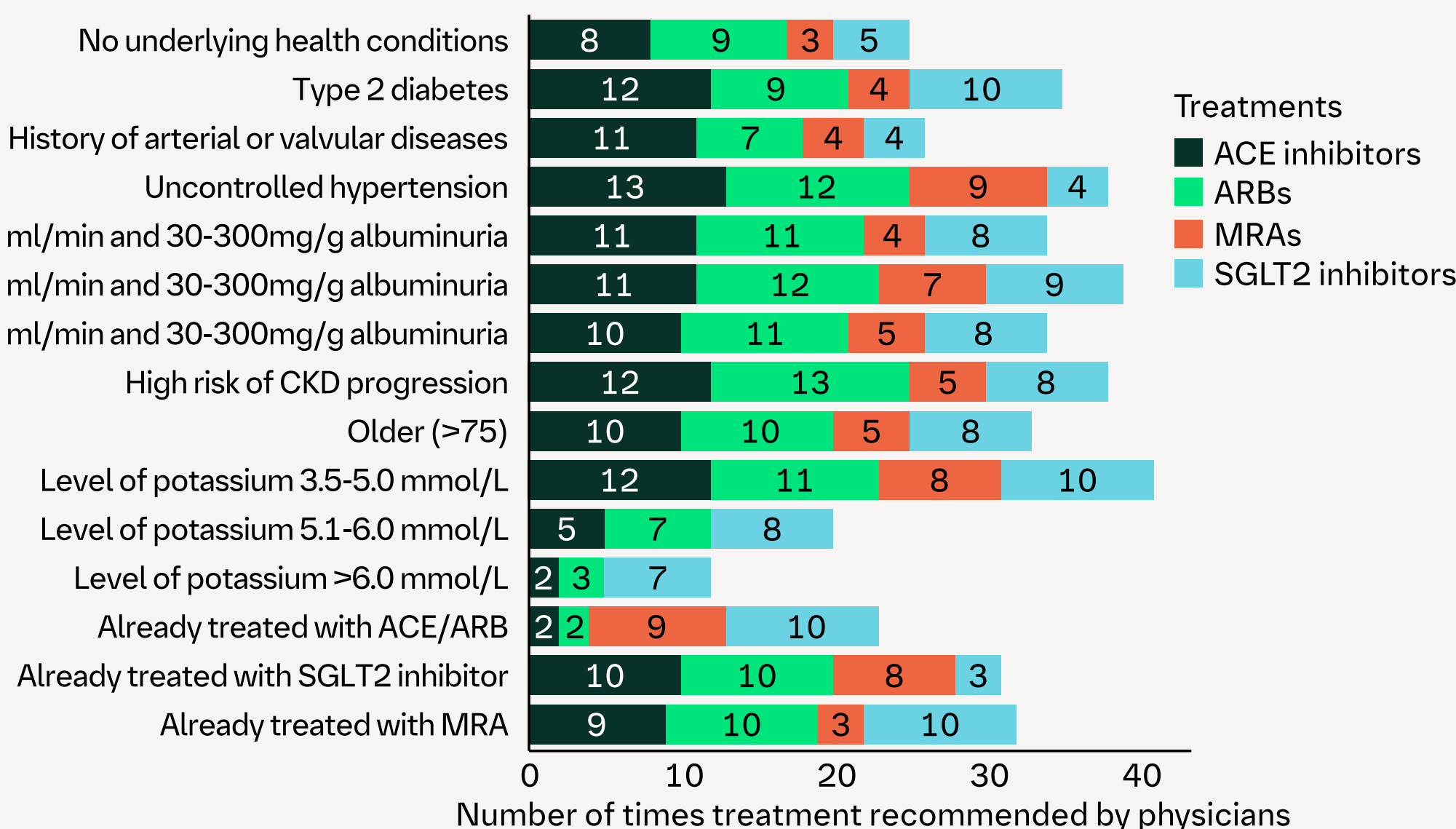
Definition of mild-to-moderate CKD and desired treatment features

- Physicians were asked to define mild-to-moderate CKD and describe unmet treatment needs.
- Mild CKD was generally defined as CKD stage 1 (n=11, 65%) and stage 2 (n=12, 71%). Moderate CKD was generally defined as CKD stage 3a (n=12, 71%) and stage 3b (n=12, 71%). Only three physicians provided specific estimated glomerular filtration rates (eGFR) and albuminuria rates to define mild-to-moderate CKD.
- Approximately half of physicians noted that the treatment feature that they would most like to see in a new treatment for mild-to-moderate CKD was slowing of CKD progression (n=8, 47%). Physicians also wanted new treatments that avoided hyperkalemia (n=6, 35%), cough (n=3, 18%), and urinary tract infections (n=3, 18%).

Patient profiles

- To understand heterogeneity across prescribing behavior, physicians were presented with 15 patient profiles and asked to identify which treatments—angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), SGLT2 inhibitors, and/or MRAs—they would prescribe for each profile.
- Most physicians indicated willingness to prescribe RAAS inhibitors (**Figure 1**) and many (n=11; 65%) considered SGLT2 inhibitors as a standalone treatment option. Greater hesitancy was observed for prescribing MRAs, especially by general practitioners.

Figure 1. Physician treatment choice by patient profile



References
1. Vaidya SR, Aeddula NR. *Chronic Kidney Disease*. StatPearls Publishing; 2024. 2. Lessey G, et al. *Vasc Health Risk Manag*. 2019;15:365-73. 3. Tarun T, et al. *Kidney Int Rep*. 2024;9(1):16-28. 4. Bianchi S, et al. *J Nephrol*. 2019;32(4):499-516. 5. Costa D, et al. *Front Med (Lausanne)*. 2023;10:1178140. 6. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppl*. 2013;3(1):1-150. 7. Cheung AK, et al. *Kidney Int*. 2021;99(3):559-69. 8. Neumiller JJ, et al. *Clin Kidney J*. 2024;17(1):sfad285. 9. Veldwijk J, et al. *Patient*. 2023;16(6):641-53.

Disclosures
The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors.
The authors did not receive payment related to the development of this poster.
KM, MQ, and AD of Evidera Ltd., a business unit of PPD, part of Thermo Fisher Scientific, conducted the research, which was contracted and funded by Boehringer Ingelheim International GmbH. JF and JB served as expert advisors on this study and are contracted and funded by Boehringer Ingelheim International GmbH.
Boehringer Ingelheim International GmbH was given the opportunity to review the manuscript for medical and scientific accuracy as well as intellectual property considerations.
The study was supported and funded by Boehringer Ingelheim International GmbH.

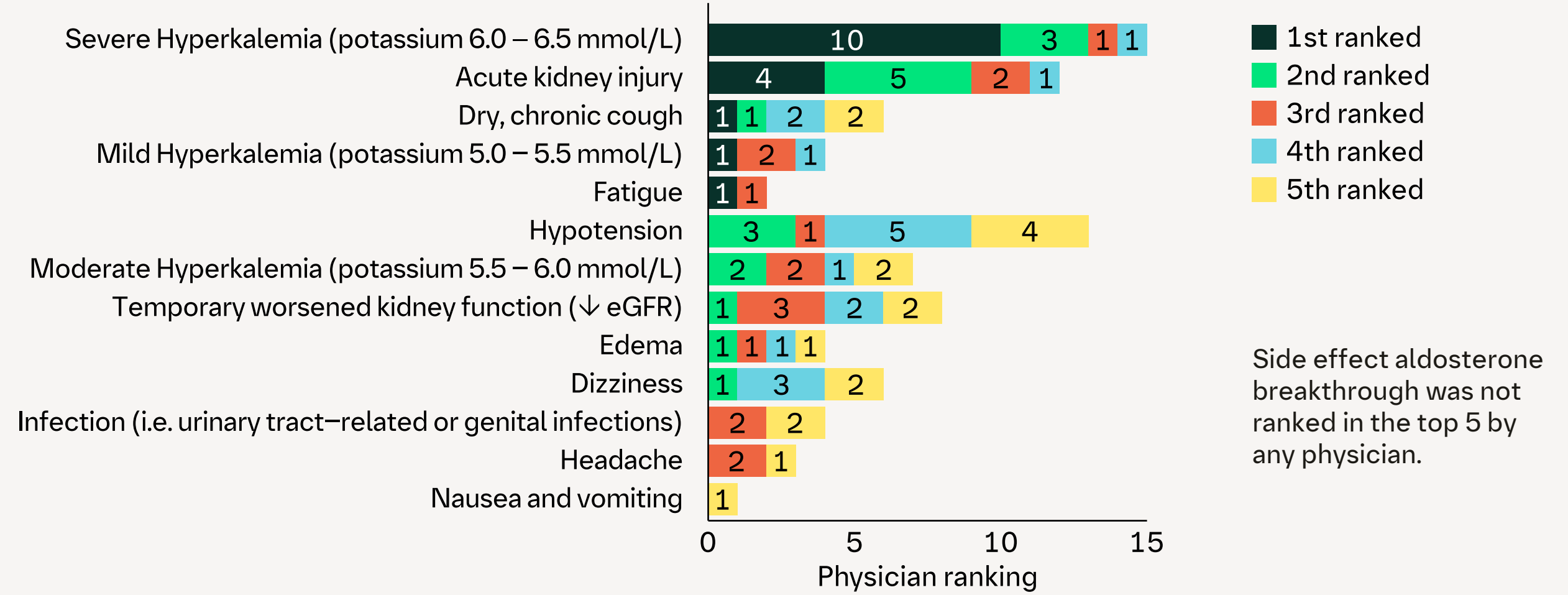
Importance of treatment side effects

- Physicians ranked the top five most important treatment side effects out of a possible 14 identified from the targeted literature review.
- Key side effects physicians sought to avoid were severe hyperkalemia (potassium ≥ 6.0 mmol/L), acute kidney injury, and hypotension (**Figure 2**).

"Severe hyperkalemia is what is life threatening."

"I hate hyperkalemia, so even mild hyperkalemia can be a problem."

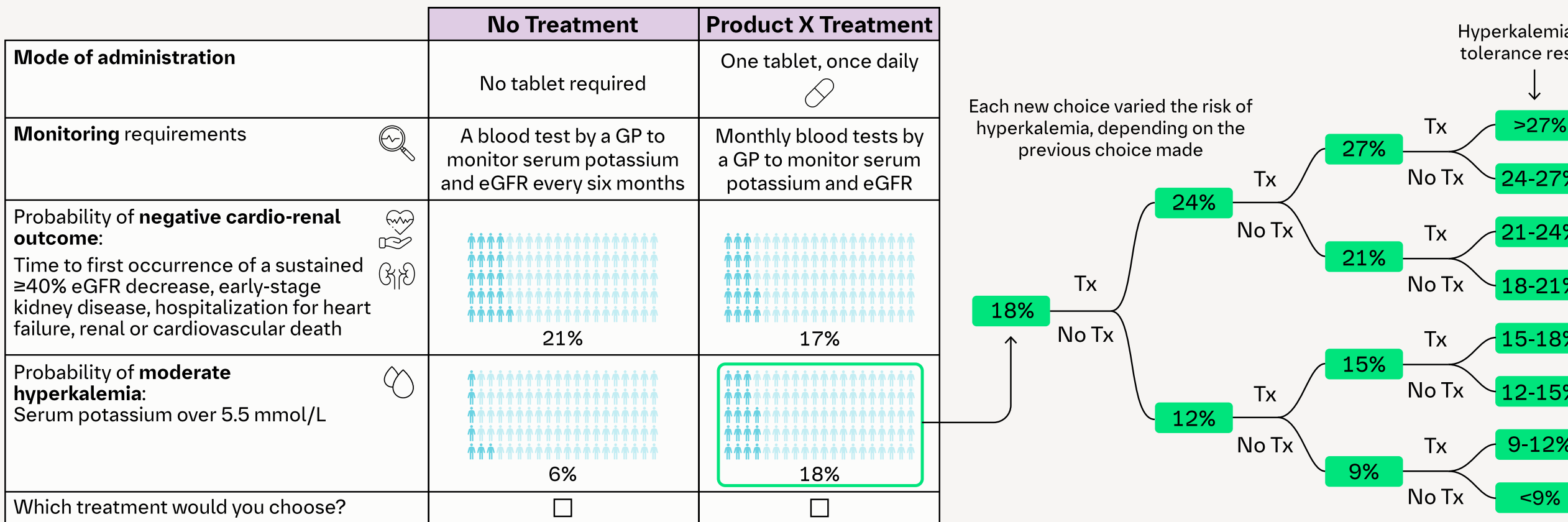
Figure 2. Physician-ranked importance of treatment side effects that should be averted



The risk of hyperkalemia

- A thresholding exercise (**Figure 3**) was conducted to give quantitative insights into the maximum acceptable risk (MAR) of hyperkalemia, defined as serum potassium over 5.5 mmol/L, that physicians were willing to tolerate in return for a moderate treatment benefit (defined as a sustained $\geq 40\%$ decrease in eGFR, early stage kidney disease, hospitalization for heart failure, renal or cardiovascular death), from 21% to 17%, i.e., a 4-percentage-point or 19% reduction in the absolute risk of cardio-renal outcomes.⁹

Figure 3. Hyperkalemia thresholding exercise and tree

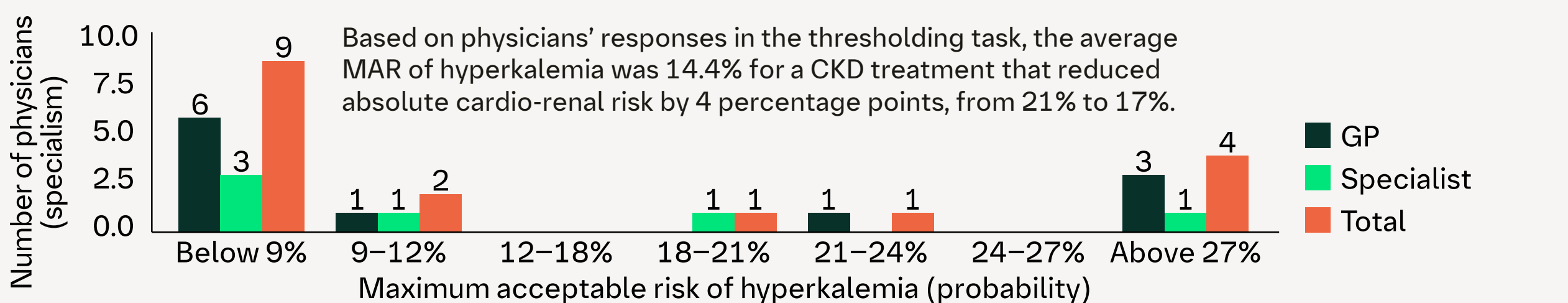


- Some physicians preferred to immediately discontinue medication that raises potassium levels, whereas others preferred to first try to manage hyperkalemia with potassium-lowering medication.

One of the six physicians who stated they would discontinue an MRA because of hyperkalemia said: "...a combination of ACE or ARB with an antagonist will quite often cause hyperkalemia and I'll have to stop the MRA."

One US physician who preferred trying to manage hyperkalemia first said: "Usually, these patients are quite ill and they're taking a lot of medications and it depends upon the severity of illness... whether I pull back on the medication that I'm prescribing, or whether I add one of the potassium lowering medications."

Figure 4. Distribution of maximum acceptable risk of hyperkalemia



Conclusions

- Decision-making across mild-to-moderate CKD treatment pathways is complex, and physicians use differing strategies toward treatment and related benefit-risk management.
- Definitions and treatment approaches varied among physicians, highlighting nonuniform attitudes and behaviors around treatment decision-making.
- There was variation across physicians in the way they balanced the benefits of slowing CKD progression with risks such as hyperkalemia.
- Features of new treatments for mild-to-moderate CKD that physicians would like to see include slowing CKD progression and avoiding hyperkalemia, cough, and urinary tract infections.
- Quantifying the trade-offs that physicians are willing to make between the benefit and risks of CKD treatment is a key avenue for future research.

Acknowledgments
The authors would like to thank John Plant, Alison Danson, and Shani Berger of Evidera Inc., a business unit of PPD, part of Thermo Fisher Scientific, for their medical writing, editorial, and graphic contributions.

Abbreviations
ACE, angiotensin-converting enzyme [inhibitor]; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GP, general practitioner; MAR, maximum acceptable risk; MRA, mineralocorticoid receptor antagonist; RAAS, renin-angiotensin-aldosterone system; SGLT2, sodium-glucose transport protein 2 [inhibitor]; Tx, treatment

