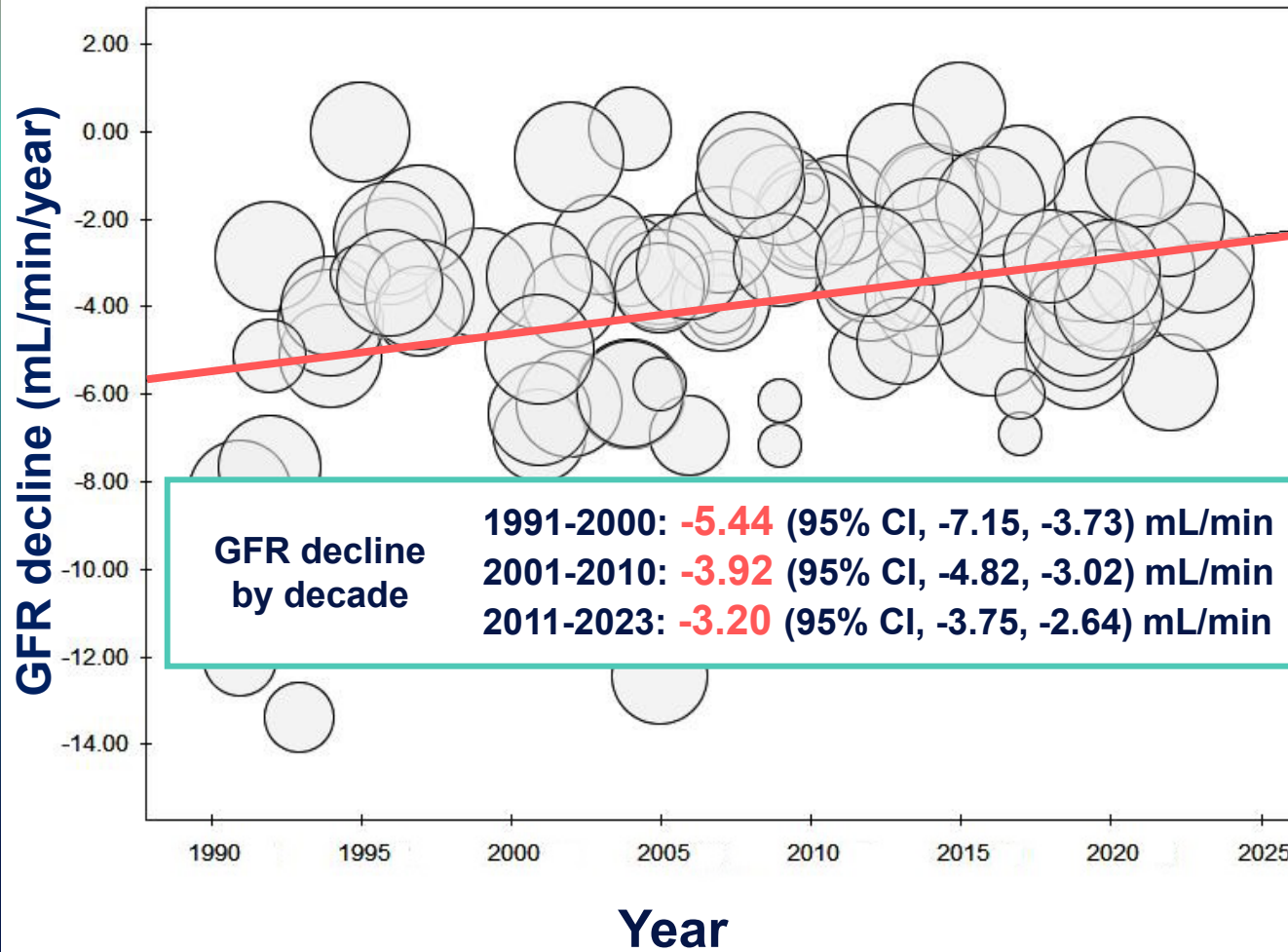


# RAASi Have Contributed to Reducing GFR Loss Over the Last 30 Years

Meta-analysis of control arms from 92 RCTs in patients with CKD



DECADES	1991-2000	2001-2010	2011-2023
Number of RCTs	20	33	39
Patients (n)	1,283	4,874	26,045
Female (%)	38	38	39
Mean age (years)	51 ± 7	55 ± 9	58 ± 10
Diabetes (%)	26	40	55
CV disease (%)	NA	42	47
Systolic BP (mmHg)	144 ± 11	141 ± 11	135 ± 8
GFR (mL/min)	35 ± 18	43 ± 20	43 ± 18
UProt (g/24h):	2.5 [1.5-3.9]	1.3 [0.8-2.5]	0.9 [0.3-1.6]
RAASi use (%)	16	59	85

BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; GFR, glomerular filtration rate; RAASi, renin-angiotensin-aldosterone system inhibitor; RCT, randomized controlled trial; Uprot, proteinuria.

Garofalo C, et al. *Am J Kidney Dis.* 2024;83(4):435-444.e1.

# Michael Böhm, MD

Only 50% of the patients with heart failure have normal kidney function



# Challenges in Managing Hyperkalemia: Cardiologist's Perspective

- The potential creation of hyperkalemia
- Fear of hyperkalemia
  - Leads to undertreatment in inpatient and outpatient settings
- Prone to develop hyperkalemia
  - Combination of drugs to treat heart failure in the presence of impaired kidney function



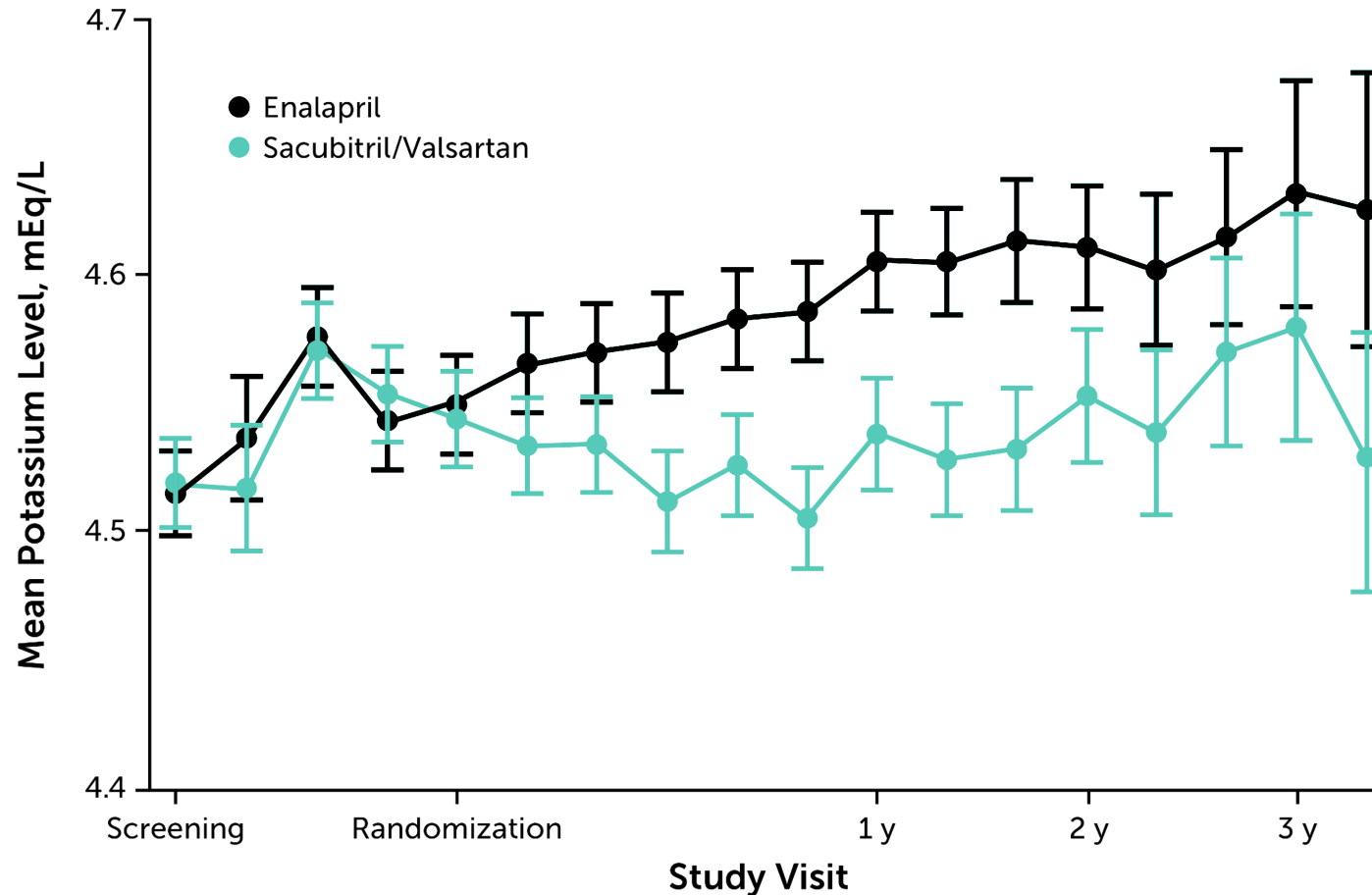
# The “Big 4”

- Guideline-directed medical treatment in heart failure
- ACEI/ARB/ARNI
- Beta-blocker
- SGLT2i
- MRA



# The PARADIGM-HF Study

Serum potassium level by study visit, according to treatment assignment, among participants treated with an MRA at baseline in PARADIGM-HF



Among MRA-treated patients with symptomatic HFrEF, severe hyperkalemia is more likely during treatment with enalapril than with sacubitril/valsartan.

HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist. Desai AS, et al. *JAMA Cardiol.* 2017;2(1):79-85.



# HF Treatment Guidelines Recommend Novel K<sup>+</sup> Binders to Treat Hyperkalemia and Enable GDMT

## 2021 ESC HF Guidelines<sup>3</sup>

**RAASi should be optimized when K<sup>+</sup> levels are <5.0 mEq/L;** closely monitor K<sup>+</sup> levels

In chronic or recurrent hyperkalemia, an approved **K<sup>+</sup>-lowering agent should be initiated** as soon as K<sup>+</sup> levels are confirmed as >5.0 mEq/L

Maintain K<sup>+</sup>-lowering agent unless alternative treatable etiology for hyperkalemia is identified



# Most studies indicate worse outcome of CKD when RAASi are discontinued...even in severe disease!!!



# KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

## Recommendations

- 3.6.1: We recommend starting renin-angiotensin-system inhibitors (RASi) (angiotensin-converting enzyme inhibitor [ACEI] or angiotensin II receptor blocker [ARB]) for people with CKD and severely increased albuminuria (G1–G4, A3) without diabetes (1B).
- 3.6.2: We suggest starting RASi (ACEI or ARB) for people with CKD and moderately increased albuminuria (G1–G4, A2) without diabetes (2C).
- 3.6.3: We recommend starting RASi (ACEI or ARB) for people with CKD and moderately to severely increased albuminuria (G1–G4, A2 and A3) with diabetes (1B).

## Practice Points

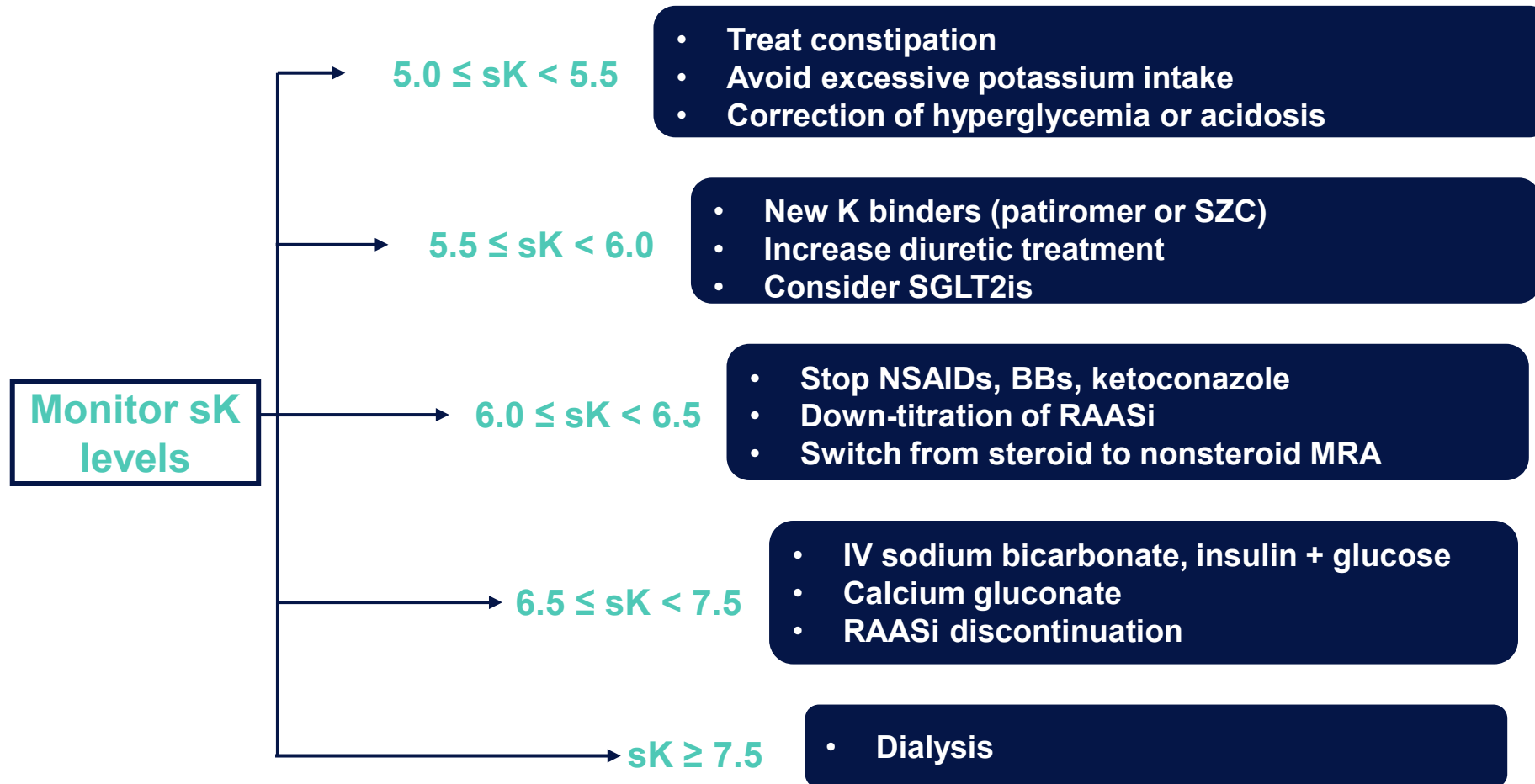
- 3.6.3: Hyperkalemia associated with use of RASi can often be managed by measures to reduce the serum potassium levels rather than decreasing the dose or stopping RASi.
- 3.6.7: Continue ACEI or ARB in people with CKD even when the eGFR falls below 30 mL/min/1.73 m<sup>2</sup>.
- **3.6.5: Consider reducing the dose or discontinuing ACEI or ARB in the setting of either symptomatic hypotension or uncontrolled hyperkalemia despite medical treatment, or to reduce uremic symptoms while treating kidney failure (estimated glomerular filtration rate [eGFR] <15 mL/min/1.73 m<sup>2</sup>).**





# Pragmatic step-by-step approach to prevent/treat hyperkalemia in CKD... ...while keeping RAASi on board as long as possible

## Intervention



BB, beta-blocker; CKD, chronic kidney disease; IV, intravenous; K, potassium; MRA, mineralocorticoid receptor antagonist; NSAID, nonsteroidal anti-inflammatory; RAASi, renin-angiotensin-aldosterone system inhibitor; SGLT2i, sodium glucose transporter type 2 inhibitor; sK, serum potassium; SZC, sodium zirconium cyclosilicate.

De Nicola L, et al. *Intern Emerg Med.* 2024;19(2):295-306.

# Keys to Collaboration: Cardiologist

- The highest comorbidity load in the elderly population with chronic heart failure is issues with the kidney
  1. Inclusion of nephrologist when hyperkalemia gets difficult or dialysis is necessary
  2. Available as kidney function declines



# Luca De Nicola, MD

Collaboration

Action



# Key Takeaways: Michael Böhm, MD

“Don't be afraid of the kidney...”

“...because we have the collaboration possibilities with the nephrologists.”

