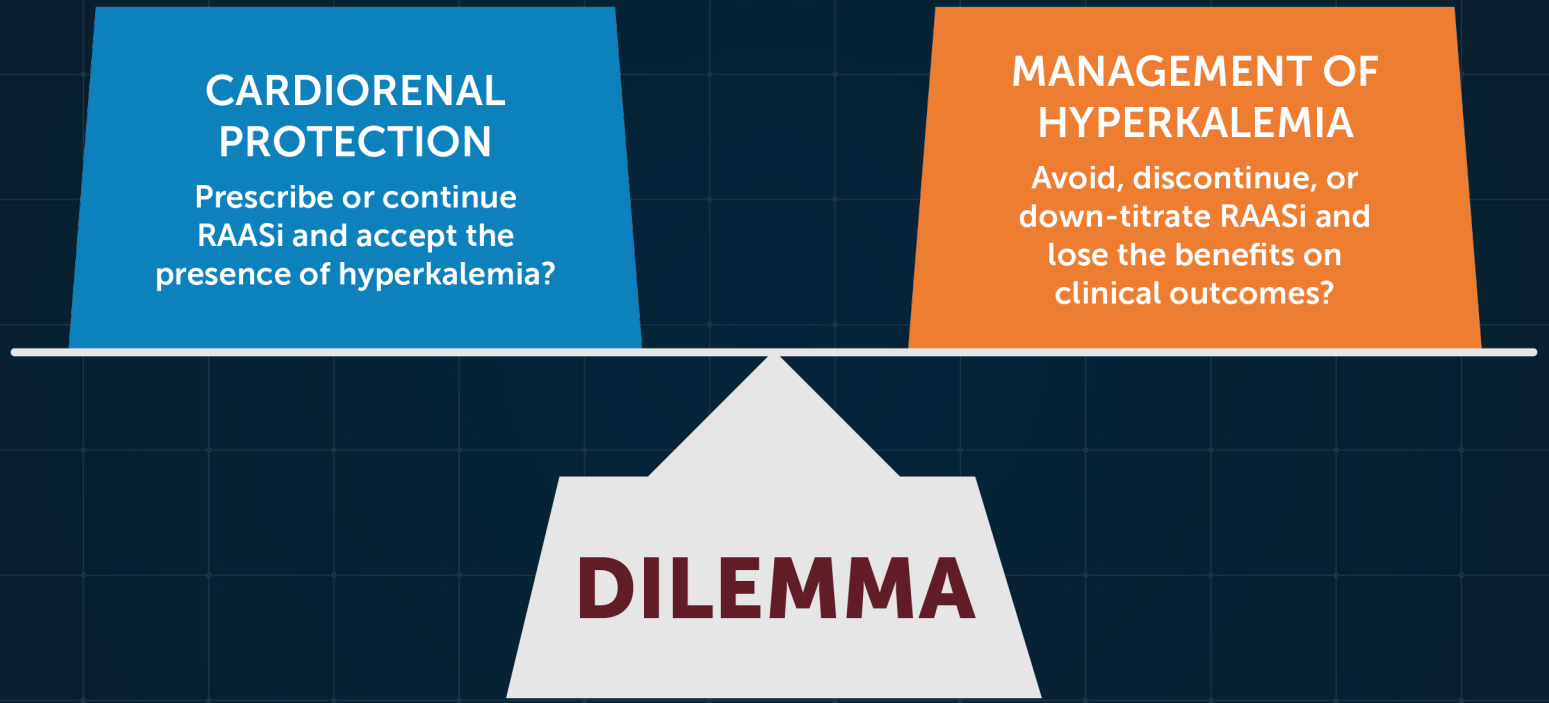
CLINICAL CASE

- 71-year-old patient recently discharged after his first hospitalization for HF (hypertensive, HFrEF, LVEF 32%)
- History of CKD (eGFR 58 mL/min/1.73 m^2), RAC 28 mg/g before HFH, under ACEI (ramipril 10 mg/d, hydrochlorothiazide 12.5 mg/d, amlodipine 10 mg/d), eGFR stable over the last 2 years
- Presenting (30 days post discharge) with:
  - NYHA class II, BP 128/82 mmHg, no orthostatic hypotension, HR 58 bpm, no pulmonary rales, no lower limb edema, “normal” JVP, stable body weight vs discharge (BMI 29 kg/m^2)
  - eGFR 48 mL/min/1.73 m^2 along with hyperkalemia 5.6 mmol/L, Na^+ 140 mmol/L, bicarb 26 mmol/L
    - Current regimen: sacubitril valsartan 97/103 bid, bisoprolol 10 mg od, dapagliflozin 10 mg od, eplerenone 25 mg od, furosemide 20 mg/d

CLINICAL CASE



CKD and HF Treatment Guidelines Recommend Novel K^+ Binders to Treat Hyperkalemia and Enable GDMT

KDIGO 2020 Clinical Practice Guideline for Diabetes Management in CKD[1]

Initiate ACEI or ARB in patients with CKD

↓

Monitor potassium within 2-4 weeks after starting or changing dose

↓ *If HK occurs:*

- Review concurrent drugs
- Moderate potassium intake
- Consider:
  - Diuretics
  - Sodium bicarbonate
  - GI cation exchangers

↓

Reduce dose or stop ACEI or ARB as last resort

KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in CKD[2]

Recommendations are aligned with KDIGO 2020 guidelines. In addition:

Improvement in K^+ control could lead to increased use of RAASi

In CKD patients receiving RAASi who develop hyperkalemia, the latter can be controlled with newer oral K^+ binders in many patients, with the effect that RAASi can be continued at the recommended dose

2021 ESC HF Guidelines[3]

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

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

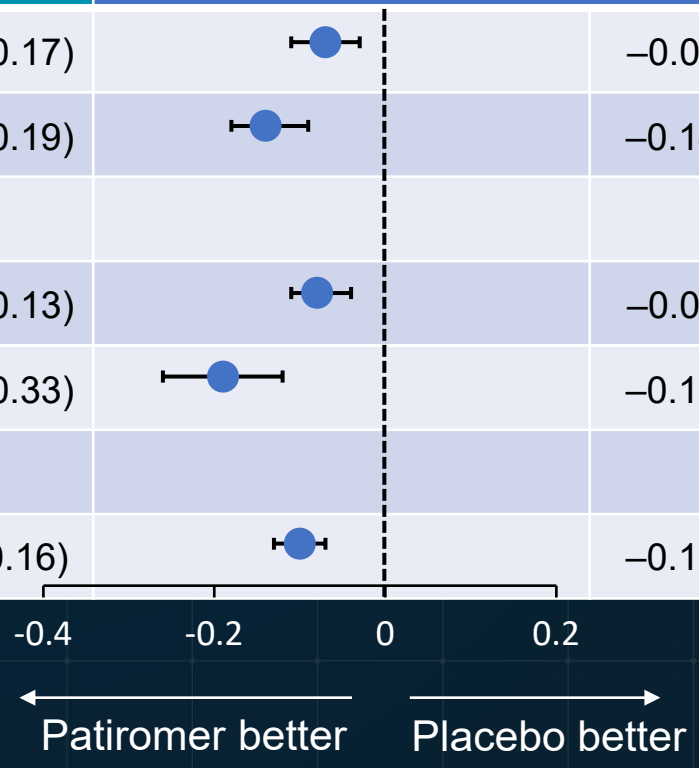
Maintain K^+-lowering agent unless alternative treatable etiology for hyperkalemia is identified

GDMT, guideline-directed medical therapy; HK, hyperkalemia; RAASi, renin-angiotensin-aldosterone system inhibitor.

1. KDIGO Diabetes Work Group. *Kidney Int*. 2020;98(4S):S1-S115. 2. KDIGO Blood Pressure Work Group. *Kidney Int*. 2021;99(3S):S1-S87.
3. McDonagh TA, et al. *Eur Heart J*. 2021;42(36):3599-3726.

Primary Outcome: Adjusted Mean Change in sK^+ Level (mEq/L) from Baseline to End of Study

Baseline eGFR subgroup	Change from baseline (95% CI)		Difference in change from baseline (95% CI)	*P* value for interaction
	Patiromer (N = 439)	Placebo (N = 439)		
≥60 mL/min/1.73m^2 (N = 227; N = 237)	0.05 (0.00; 0.10)	0.12 (0.07; 0.17)	–0.07 (–0.11; –0.03)	0.027
<60 mL/min/1.73m^2 (N = 212; N = 202)	0.00 (–0.05; 0.06)	0.14 (0.08; 0.19)	–0.14 (–0.18; –0.09)	
≥45 mL/min/1.73m^2 (N = 321; N = 347)	0.02 (–0.03; 0.06)	0.09 (0.05; 0.13)	–0.08 (–0.11; –0.04)	0.003
<45 mL/min/1.73m^2 (N = 118; N = 92)	0.06 (–0.02; 0.14)	0.25 (0.17; 0.33)	–0.19 (–0.26; –0.12)	
Overall	0.03 (–0.01; 0.07)	0.13 (0.09; 0.16)	–0.10 (–0.13; –0.07)	

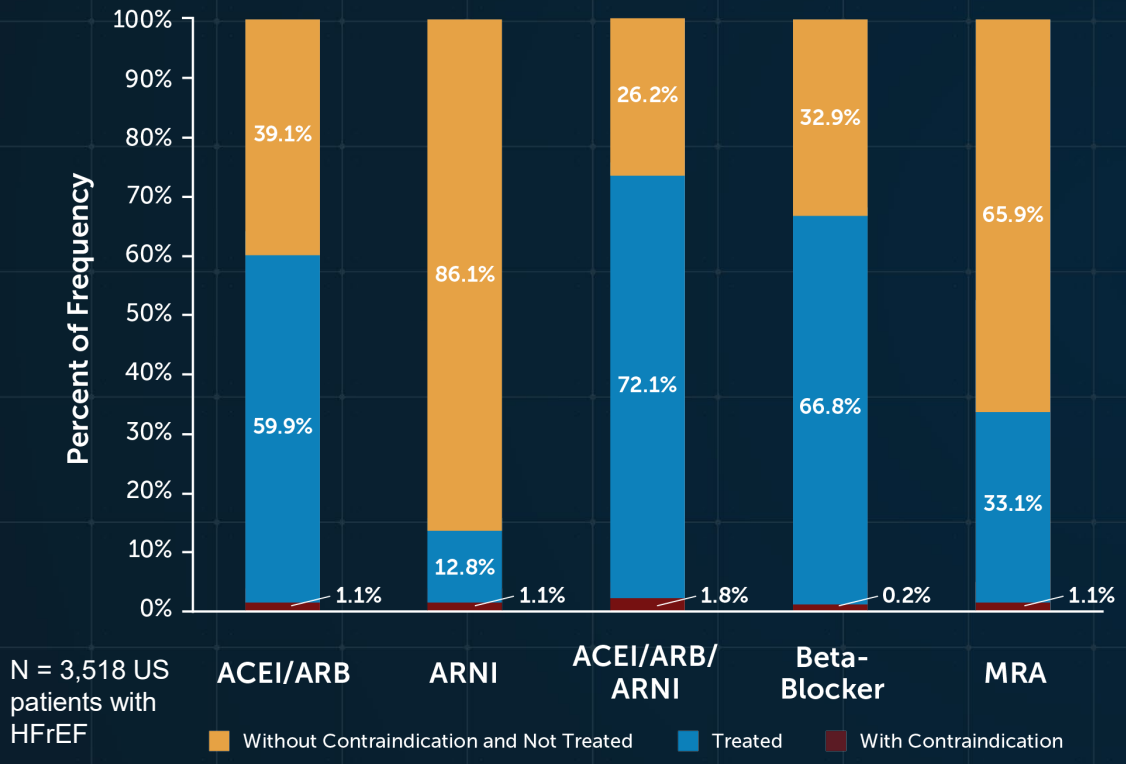


eGFR, estimated glomerular filtration rate; sK^+, serum potassium.

Butler J, et al. *Eur J Heart Fail*. 2022;43(41):4362-4373.

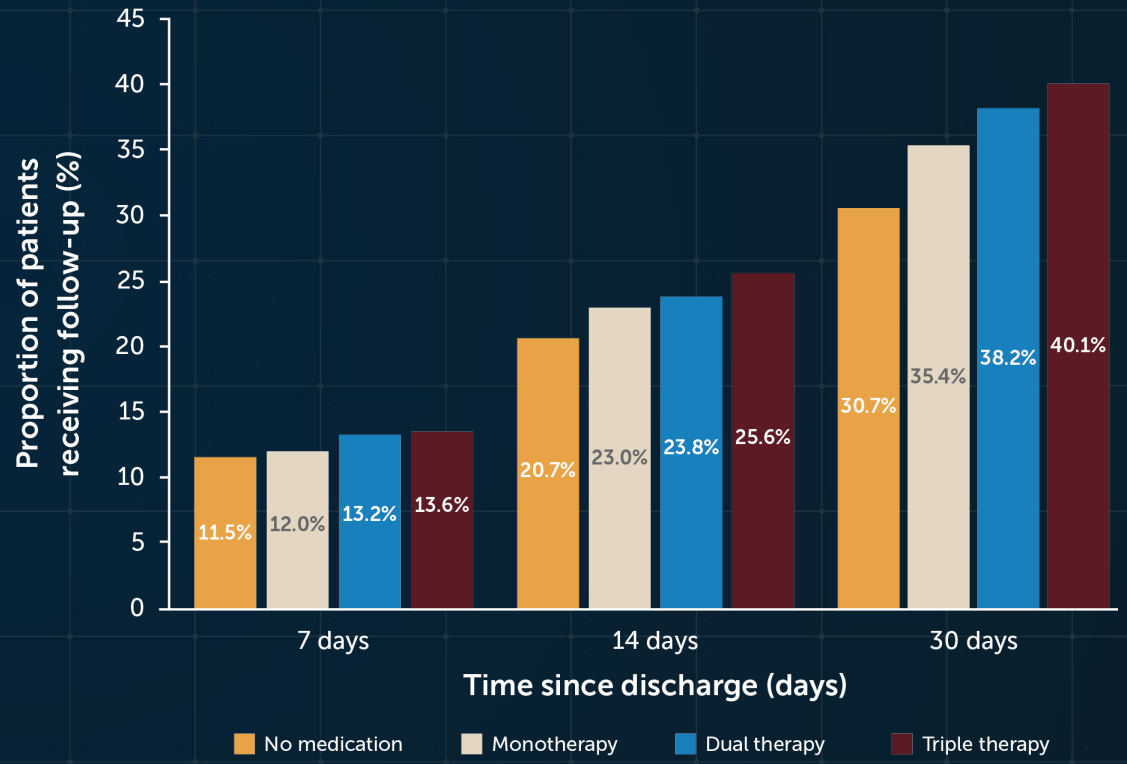
Low Rates of Guideline-Directed RAASi Therapy in HF

CHAMP-HF Registry



N = 3,518 US patients with HFrEF

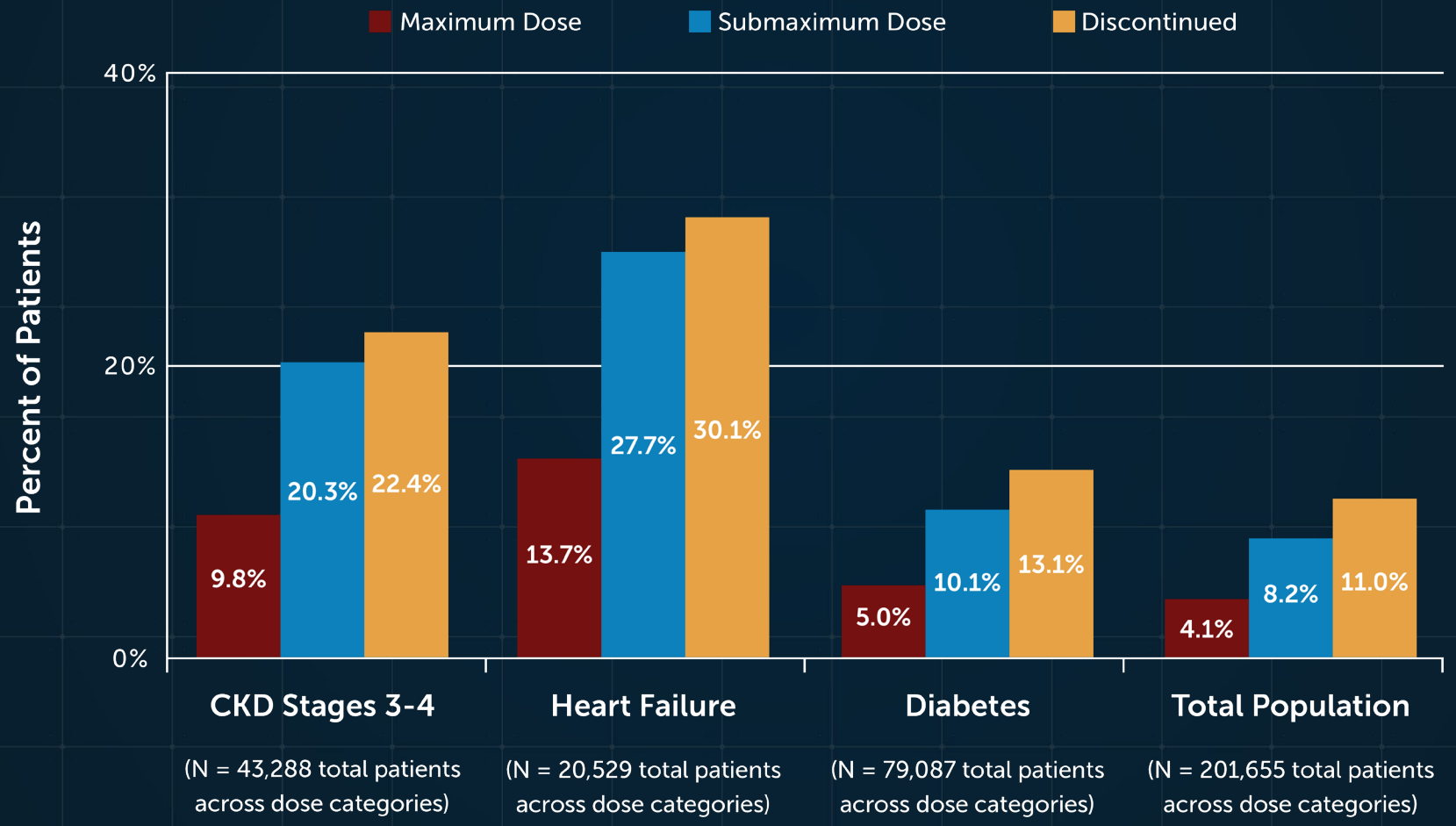
GWTG-HF Registry



ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; RAASi, renin-angiotensin-aldosterone system inhibitor.

Greene SJ, et al. *J Am Coll Cardiol*. 2018;72(4):351-366. Wirtz HS, et al. *J Am Heart Assoc*. 2020;9(16):e015042.

Suboptimal MRA Therapy Is Associated with Increased Mortality



CKD, chronic kidney disease; MRA, mineralocorticoid receptor antagonist.

Epstein M, et al. *Am J Manag Care*. 2015;21(11 Suppl):S212-S220.