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Balancing Therapies in Patients with Hyperkalemia and Heart Failure

Presenter

Speaker: Lynsey Mahlum ANP CHFN

Disclosures: None

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Objectives

1. Identify the causes and consequences of hyperkalemia for patients with heart failure.
2. List the normal range of blood potassium, and the levels measured that would indicate a patient that is hypokalemic or hyperkalemic.
3. Describe best practice recommendations regarding the use of RAAS inhibitors and potassium binders in the management of patients with comorbid conditions including heart failure, CVD and chronic kidney disease.
4. Using case studies, describe the role of shared decision-making in the current treatment options for hyperkalemia

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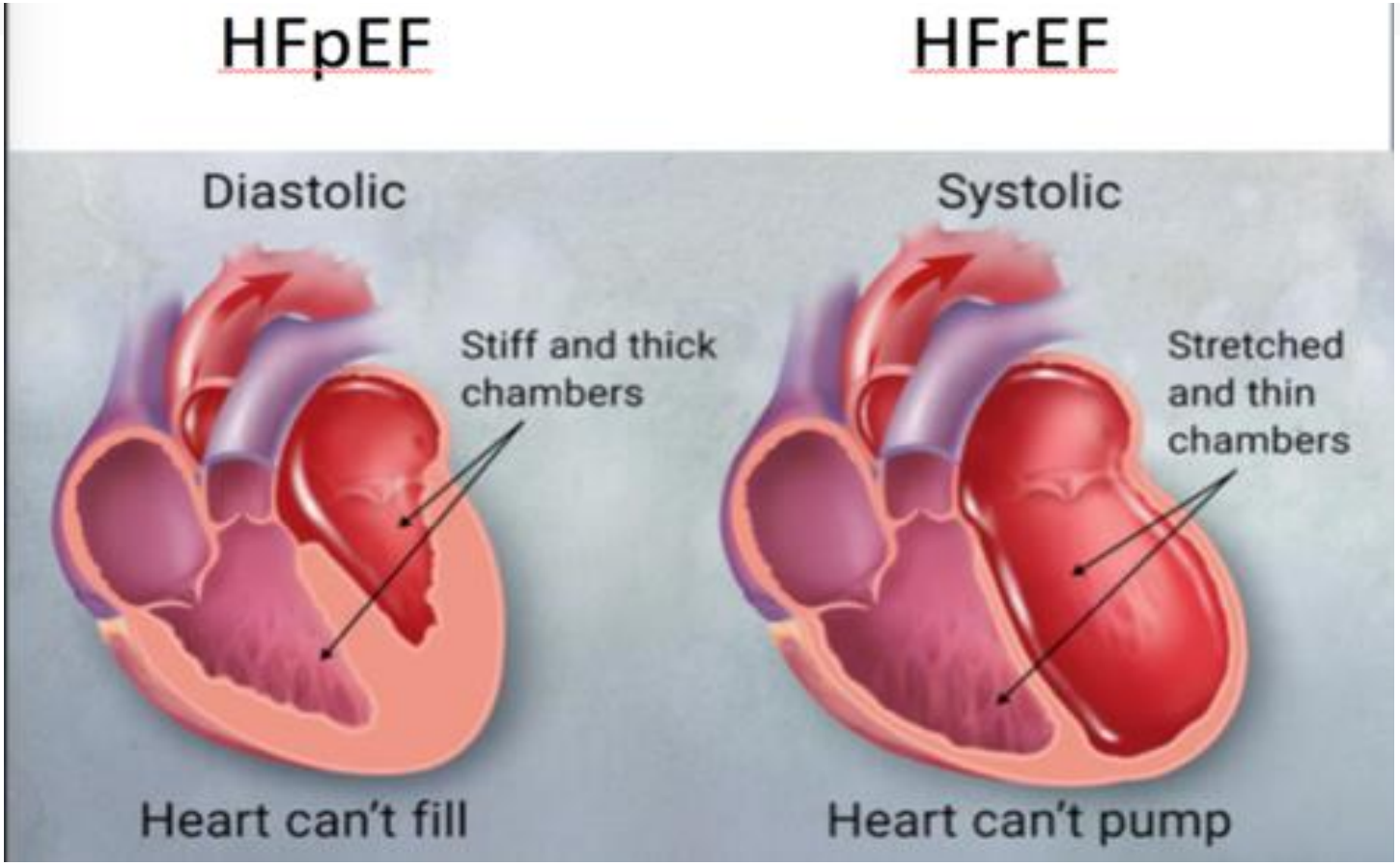
Heart Failure Subtypes

HF with <u>Preserved</u> Ejection Fraction **HF with <u>Reduced</u> Ejection Fraction**



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https://quizlet.com/101258231/pathophysiology-chapter-19-heart-failure-dysrhythmias-common-sequelae-of-cardiac-diseases-flash-cards/

Heart Failure Statistics

HF prevalence has increased from 5.7 million (2009 to 2012) to 6.5 million (2011 to 2014)

Five-year survival of HF diagnosis after an MI improved from 54% to 61%

In HF hospitalizations, 53% had HFrEF and 47% had HFpEF

- Black males = 70% of hospitalized HFrEF
- White females = 59% of hospitalized HFpEF

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Heart Disease and Stroke Statistics 2017 Update- Summary; Circulation. 2017;135:00–00

Pharmacotherapies for HFrEF

- Angiotensin Converting Enzyme Inhibitors (ACE-I)
- Angiotensin Receptor Blockers (ARB)
- Angiotensin Receptor Neprilysin Inhibitor (ARNI)*
- Beta Blockers
- Aldosterone antagonist
- Hydralazine/Nitrate
- Diuretics
- Funny-Channel Blockers*

* Unfortunately, we don't have
good data on medications
specific to HFpEF – control risk factors!

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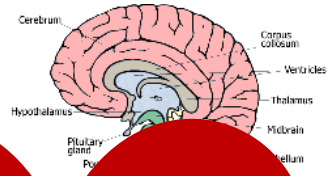
Where Do the Medications Work?

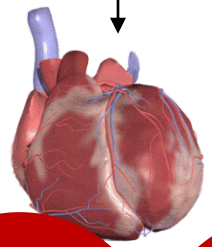
Baroreceptor response

R-A-A-S activation
Decreased GFR

Ventricular wall tension
Goal: increase SV



Kidney



Beta Blockers

•ACE/ARB
•Aldosterone Antagonist
•Sacubitril/ARB

Funny Channel Blocker

Heart Rate
Contractility

Myocyte growth

Hypertrophy

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Adapted from https://quizlet.com/101258231/pathophysiology-chapter-19-heart-failure-dysrhythmias-common-sequelae-of-cardiac-diseases-flash-cards/

Causes of Hyperkalemia

1. Inherent Hyperkalemia: includes hormonal disorders (Addison's disease, hyporeninemic hypoaldosteronism), DM, CKD and disease with cell membrane instability that can cause intracellular and extracellular potassium shifts
2. Treatment-related Hyperkalemia: medications (RAASi, MRA, NSAIDs, diuretics, Digoxin, Heparin)
3. Excess dietary intake of foods high in potassium or sodium supplements

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Which food yields the highest mg of daily value of Potassium?

- A. Avocado
- B. Banana
- C. Squash
- D. Salmon

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Signs and Symptoms of Hyperkalemia

- Patients may be asymptomatic or report the following:
- *Generalized fatigue *Weakness *Paresthesias *Paralysis *Palpitations
- Hyperkalemia can be difficult to diagnose clinically because complaints may be vague.

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Consequences of Hyperkalemia in HF patients

- Associated risk for arrhythmias and conduction system abnormalities
- Hyperkalemia frequently is discovered as an incidental laboratory finding or ECG abnormality
- decrease in speed conduction, QRS enlargement, ventricular arrhythmias, and asystole

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What organ is responsible for excreting 90% of the potassium consumed daily?

- A. Brain
- B. Liver
- C. Kidneys
- D. Skin

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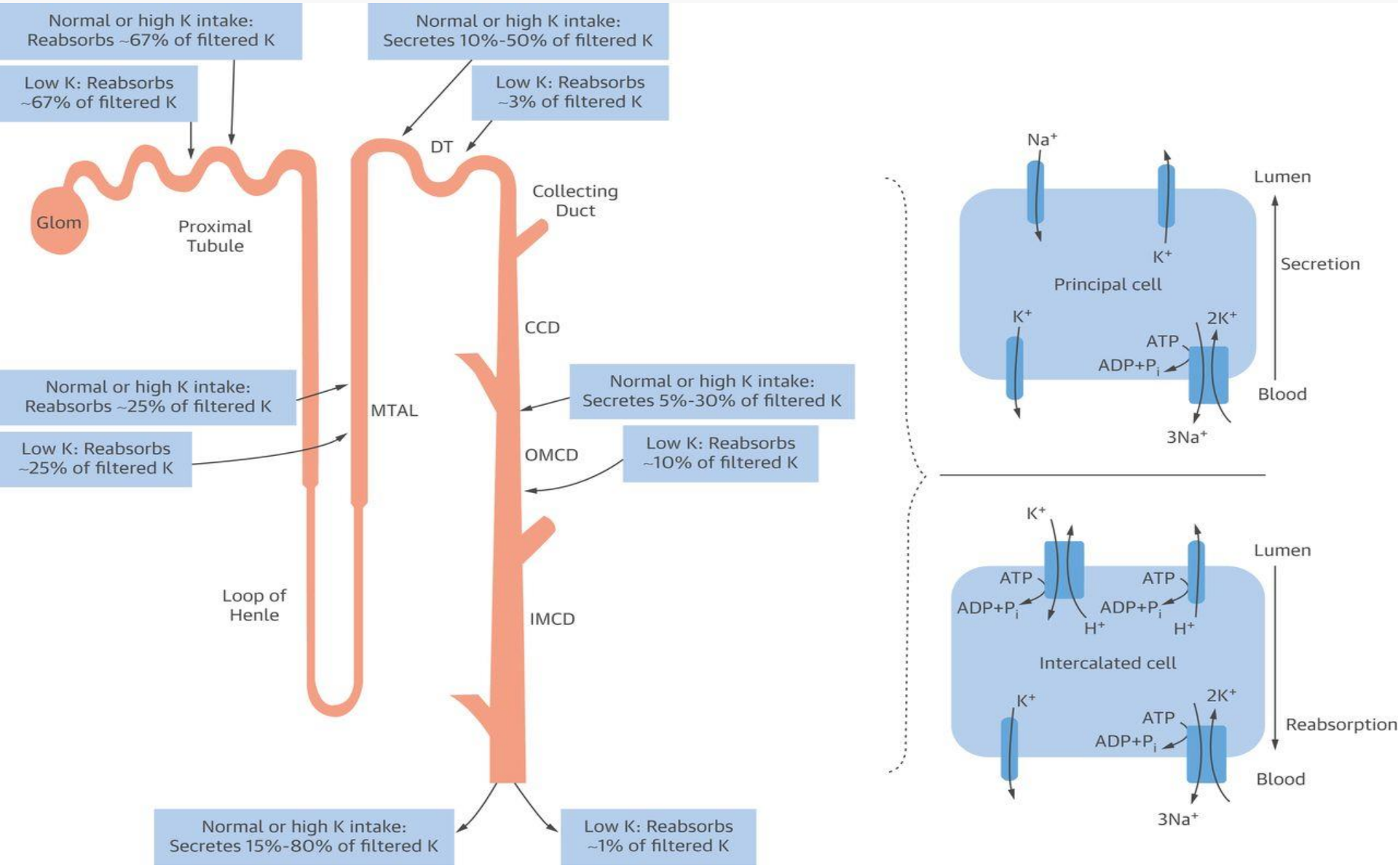

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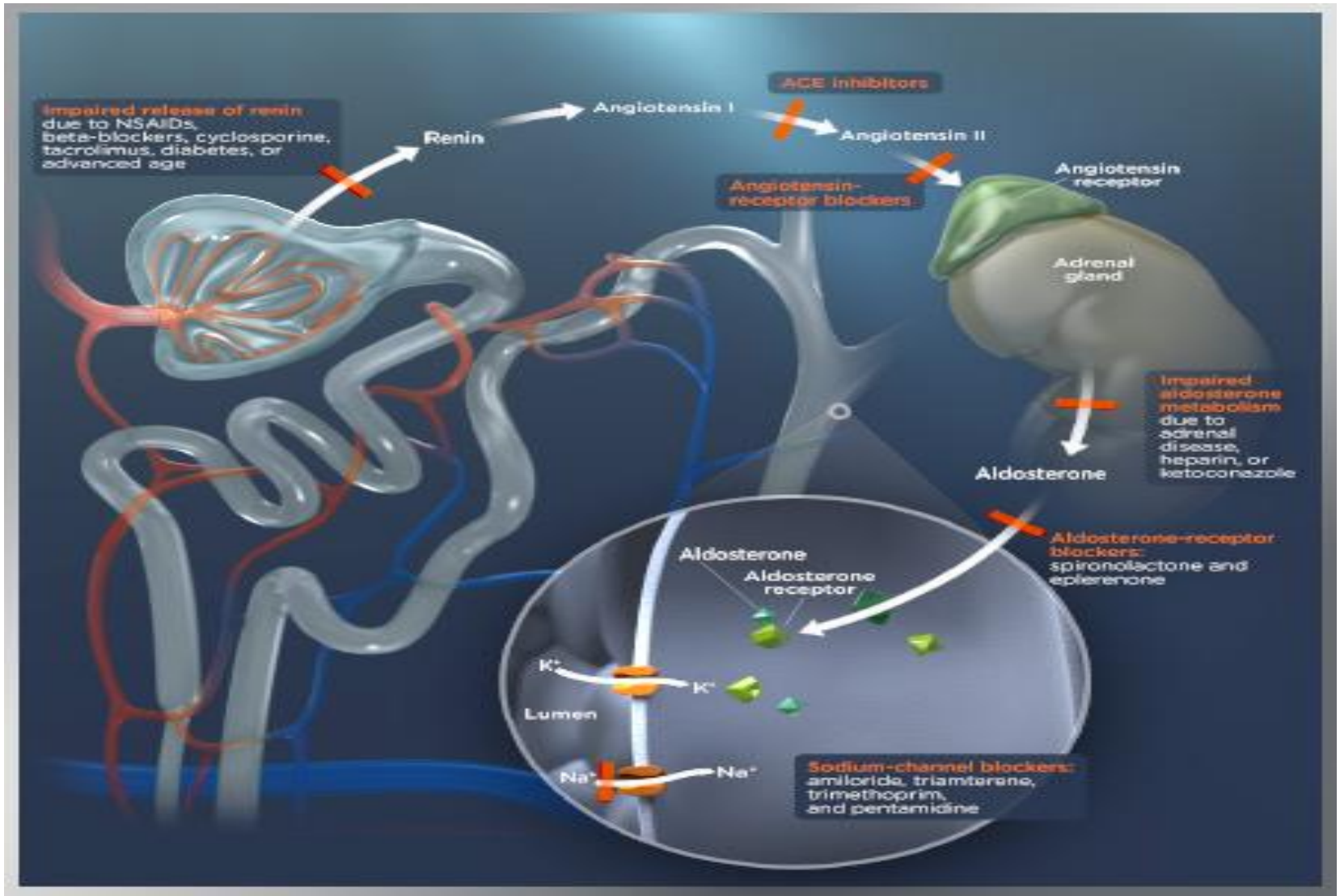
Key principles in the development of hyperkalemia



Clinical Studies

- RALES Study: Hyperkalemia rates increased with spironolactone use among heart failure patients
- EPHESUS Study: Increased risk of hyperkalemia associated with eplerenone use in heart failure patients
- RALES/EMPHASIS rates vs real-world rates: Real-world hyperkalemia rates shown to be higher with RAASi use in heart failure patients
- RENAAL Study: Increased risk of adverse kidney outcomes with losartan use among type 2 diabetes mellitus patients

What laboratory level of Potassium would you consider normal?

Hypokalemia?

Hyperkalemia?

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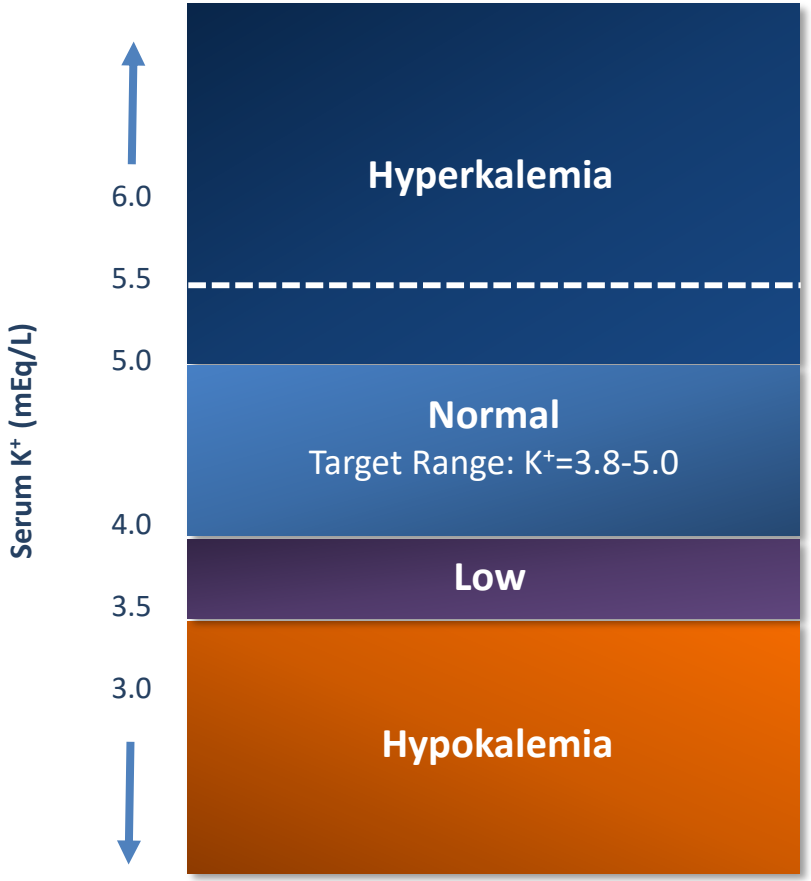
Hyperkalemia Varies Widely in Studies and Guidelines



The upper limit of normal (ULN) for serum K^+ levels varies across guidelines and publications[1-6]

- Serum K^+ levels of 5.0, 5.5, or 6.0 mEq/L are commonly used cutoffs for ULN

Some studies differentiate hyperkalemia by severity[1]

- Serum K^+ levels ≥5.5-<6.0 mEq/L defined as moderate
- Serum K^+ levels ≥6.0 mEq/L defined as severe

K^+: potassium

1. Einhorn LM, et al. *Arch Intern Med*. 2009;169(12):1156-1162. 2. Yancy CW, et al. *J Am Coll Cardiol.* 2017 Apr 21. pii: S0735-1097(17)37087-0. doi: 10.1016/j.jacc.2017.04.025.
[Epub ahead of print]. 3. Ponikowski P, et al. *Eur Heart J.* 2016;37(27):2129-2200. 4. National Kidney Foundation. Guideline 11: Use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in CKD. In: K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. 2002. http://www2.kidney.org/professionals/kdoqi/guidelines_bp/guide_11.htm. Accessed February 17, 2015. 5. National Institute for Health and Clinical Excellence (NICE) [UK]. Chronic kidney disease (CG73): Early identification and management of chronic kidney disease in adults in primary and secondary care. 2008. http://www.nice.org.uk/CG73. 6. Heart Failure Society of America, Lindenfeld J, et al. *J Card Fail*. 2010;16(6):475-539.

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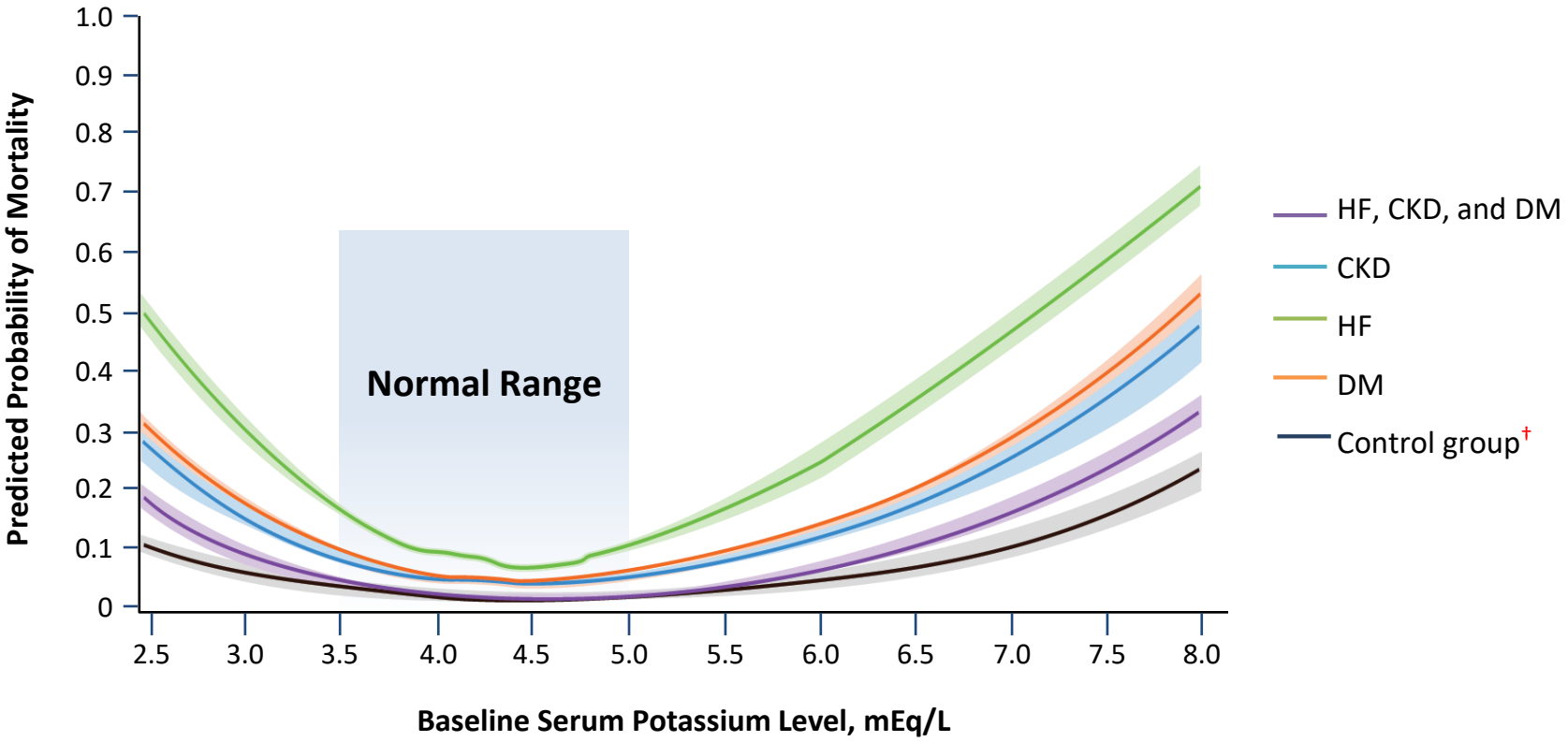
Adjusted Mortality* by Serum K^+ Level in Patients 45 to 64 Years and ≥65 Years With and Without Comorbid Illness



Increases in mortality remained after adjustments for demographic characteristics and comorbidities

CKD: chronic kidney disease; DM: diabetes mellitus; HF: heart failure; K^+: potassium.

*Evaluated through de-identified medical records (2007-2012) of individuals with ≥2 mEq/L serum K^+ readings (Humedica, Cambridge, MA). Spline analyses were performed to assess mortality at 0.1 mEq/L increments of serum K^+ after adjusting for covariates and interactions. Comorbid patients are those with diabetes, heart failure, CKD stages 3-5, cardiovascular disease, or hypertension.

†The control group comprised individuals without known HF, CVD, DM, CVD, or HTN.

Collins AJ, et al. *Am J Nephrol.* 2017;46:213-221.

Guideline Directed Medical Therapy

HFrEF (EF <40%) patients:

A. BB
B. ACE, ARB, ARNI
C. MRA
D. Diuretic

Which GDMT medications can cause Hyperkalemia?

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Guideline Directed Medical Therapy

- ACEi is attributed to the development of hyperkalemia in 10% to 38% of **hospitalized** patients, whereas hyperkalemia develops in up to 10% of the **outpatient** population within 1 year of prescribing RAASi.
- Patients with impaired renal function and diabetes are at higher risk of hyperkalemia.

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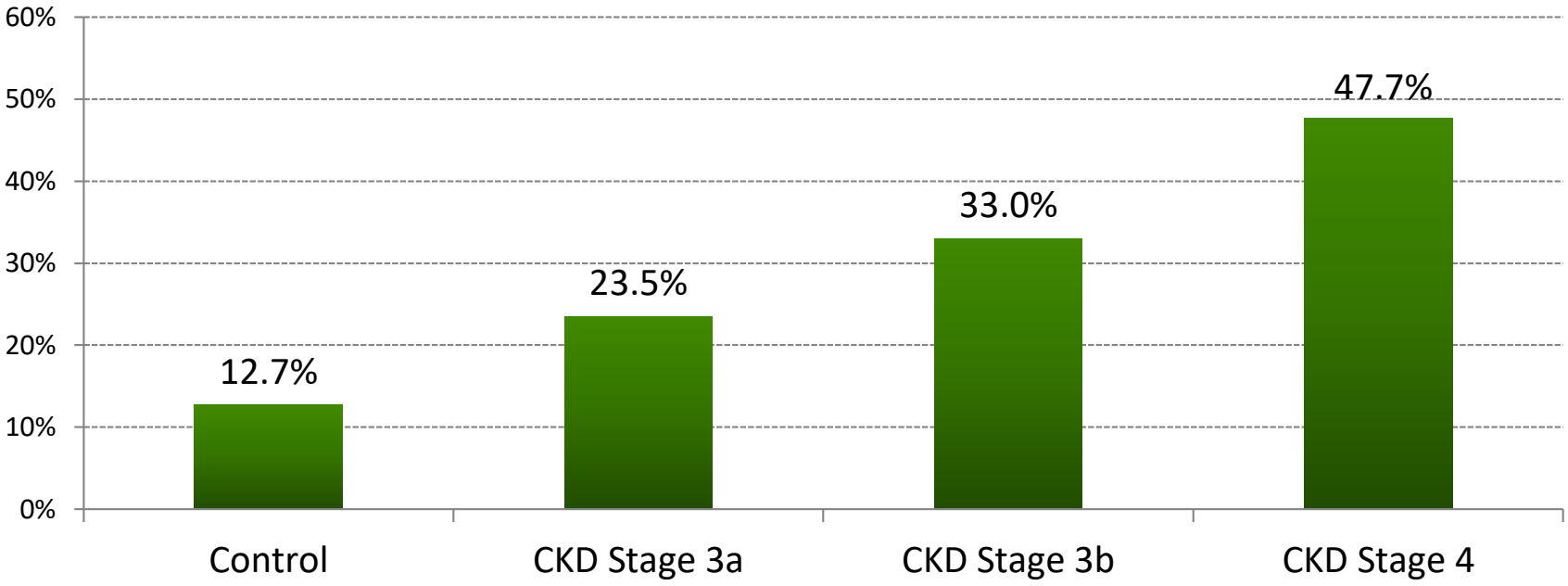
Hyperkalemia Is Prevalent Among Older Populations With Advanced Kidney Disease

5-Year Database Prevalence of Hyperkalemia
Control Population vs CKD Stages 3a, 3b, and 4 in Patients ≥65 Years



CKD: chronic kidney disease; K^+: potassium.
Based on analysis of 1.63 million persons aged ≥5 years with potassium readings on 2 dates (2008-2012), with >1 K^+ value between 2.5 and 10 mEq/L during 2008-2012. Control population composed of patients ≥65 years without CKD stages 2-5, heart failure, diabetes, or end-stage renal disease (ESRD).
Hyperkalemia defined as highest reported potassium value ≥5.1 mEq/L in 2008-2012.
Data on file. Relypsa, Inc., Redwood City, CA. Data source: Humedica, Cambridge, MA.

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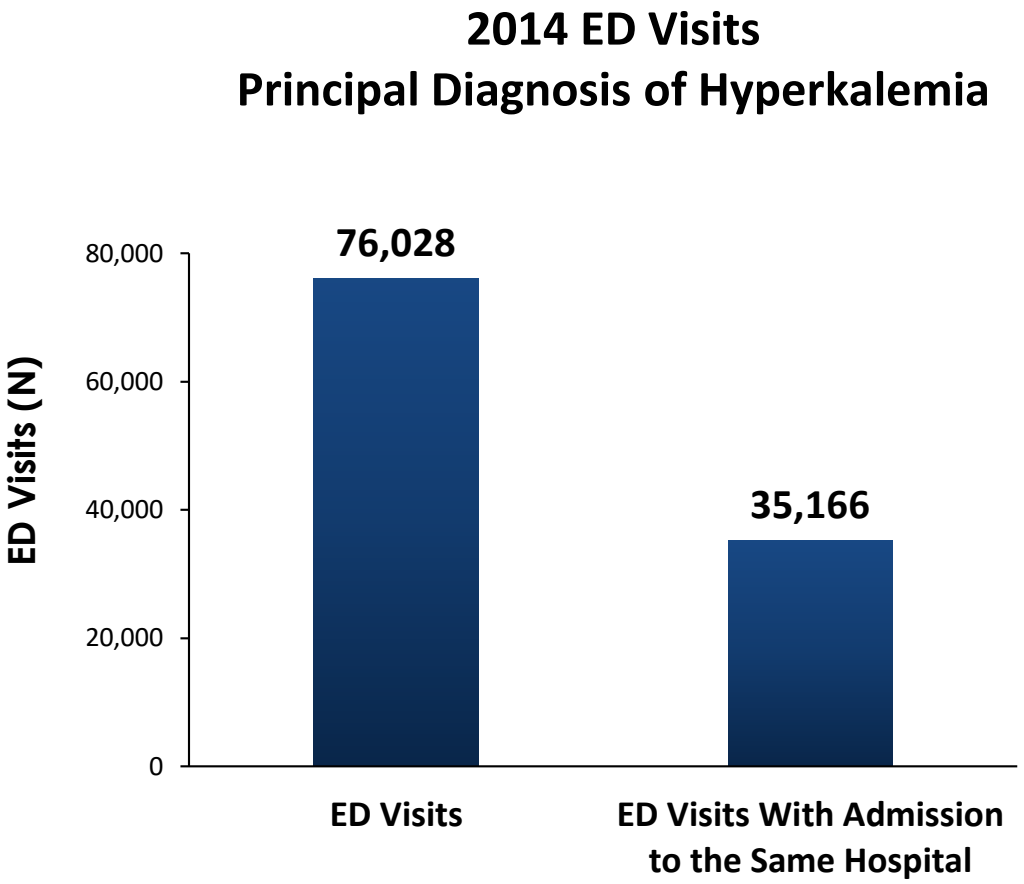
Hyperkalemia Contributes to More Than 75,000 ED Visits Annually and Represents a Financial Burden to the US



2014

> 1 Million hospital discharges with hyperkalemia listed as **any diagnosis**

Average **length of hospital stay** for a primary diagnosis of hyperkalemia was **3.3 days**

Mean charges per hospital stay were **$29,181**

Aggregate charges for hospitalization were **~$1.2 Billion**

ED: emergency department.

Healthcare Cost and Utilization Project (HCUP). 2014. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project. http://hcupnet.ahrq.gov/HCUPnet.jsp. Accessed May 24, 2017.

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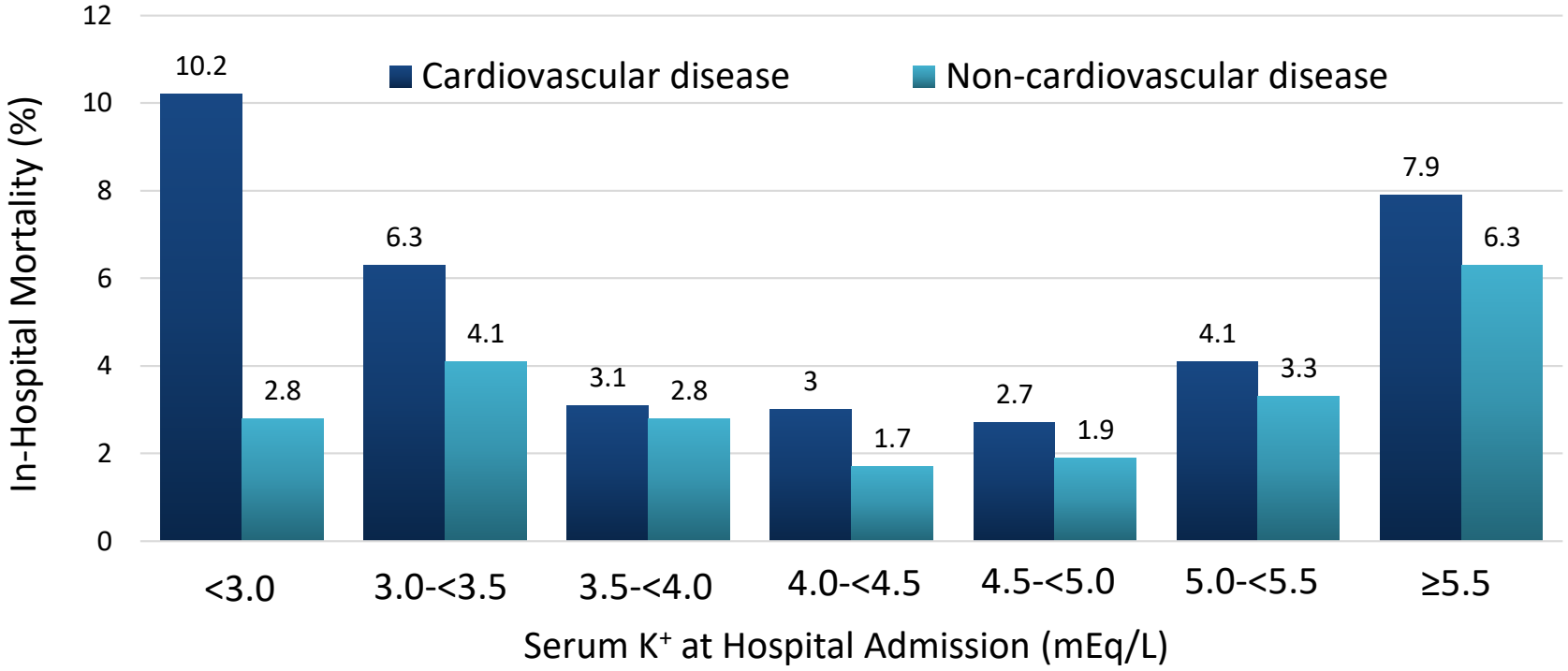
Admission Serum K^+ Levels and In-Hospital Mortality Among CKD Patients With and Without CVD

Analysis of 73,983 patients admitted to Mayo Clinic Rochester

A U-shaped curve showed higher in-hospital mortality associated with both hypo- and hyperkalemia



Odds ratio for in-hospital mortality after adjusting for potential cofounders*	3.26 (95% CI 2.03-4.98)	2.40 (95%CI 1.89-3.04)	1.38 (95% CI 1.15-1.66)	1 (REFERENCE)	1.13 (95% CI 0.94-1.37)	1.89 (95% CI 1.49-2.38)	3.62 (95%CI 2.73-4.76)

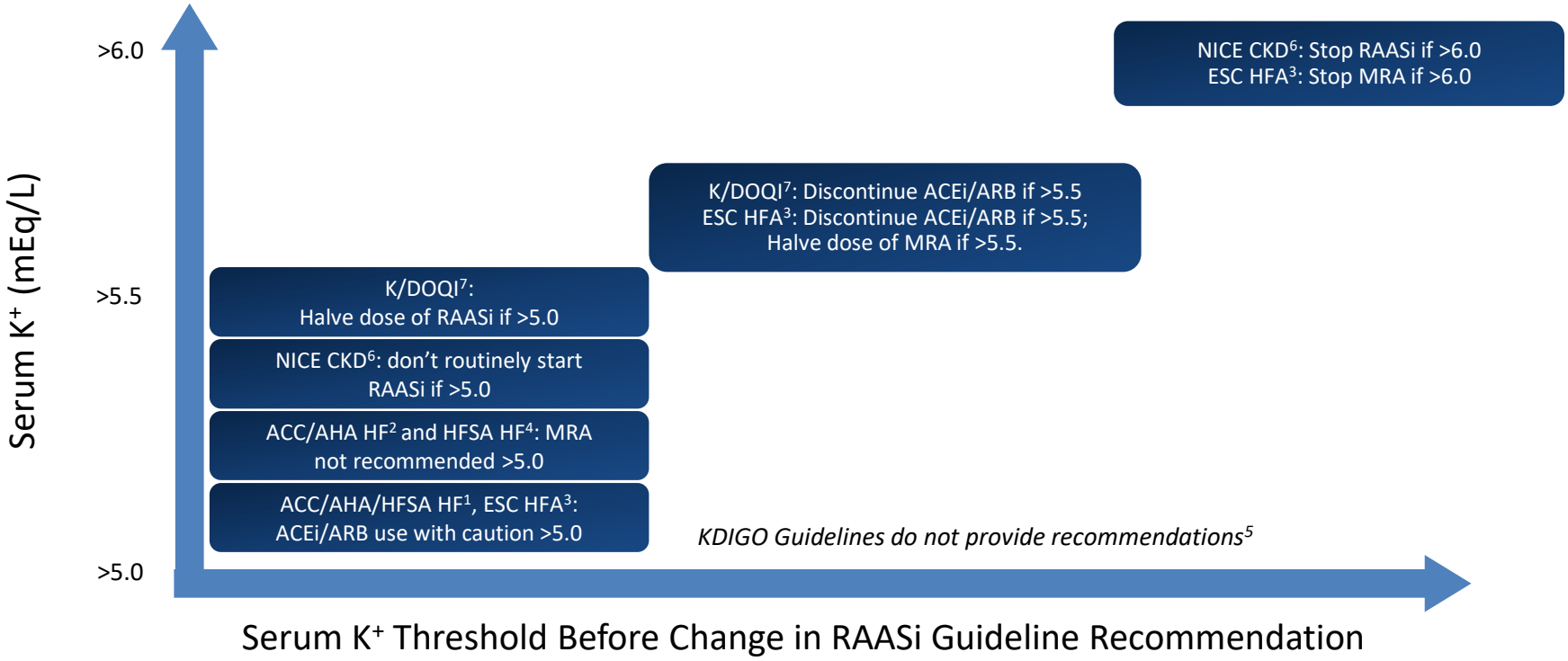
*Adjusted for age, sex, race, GFR, principal diagnosis, Charlson comorbidity score, CAD, CHF, PVD, stroke, DM, COPD, cirrhosis, and use of ACEI/ARB, diuretics, and K^+ supplements.

ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker; CAD: coronary artery disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; DM: diabetes mellitus; GFR: glomerular filtration rate; K^+: potassium; PVD: peripheral vascular disease.

Figure from Cheungpasitporn W, et al. Impact of admission serum potassium on mortality in patients with chronic kidney disease and cardiovascular disease. *QJM.* 2017 Jun 16. doi: 10.1093/qjmed/hcx118. [Epub ahead of print], by permission of Oxford University Press on behalf of the Association of Physicians.

Cheungpasitporn W., et al., *QJM*. 2017 Jun 16. doi: 10.1093/qjmed/hcx118. [Epub ahead of print]

Guidelines Recommend RAASi Dose Modifications With Increasing Serum K^+



Data from 205,108 patients from the Humedica data base indicate that

- *Few patients are prescribed maximum dose of RAASi (~20% across various cardiorenal/diabetes comorbidities)*
- *Hyperkalemia associated with RAASi therapy was frequently followed by reduction in dosage or discontinuation of therapy*
- *Patients on maximum doses of RAASi therapies experienced fewer cardiorenal adverse outcomes or mortality compared with patients on submaximum doses or who discontinued RAASi.*
  - *Adverse outcomes included mortality, ESRD, stroke, acute myocardial infarction, and coronary revascularization.*

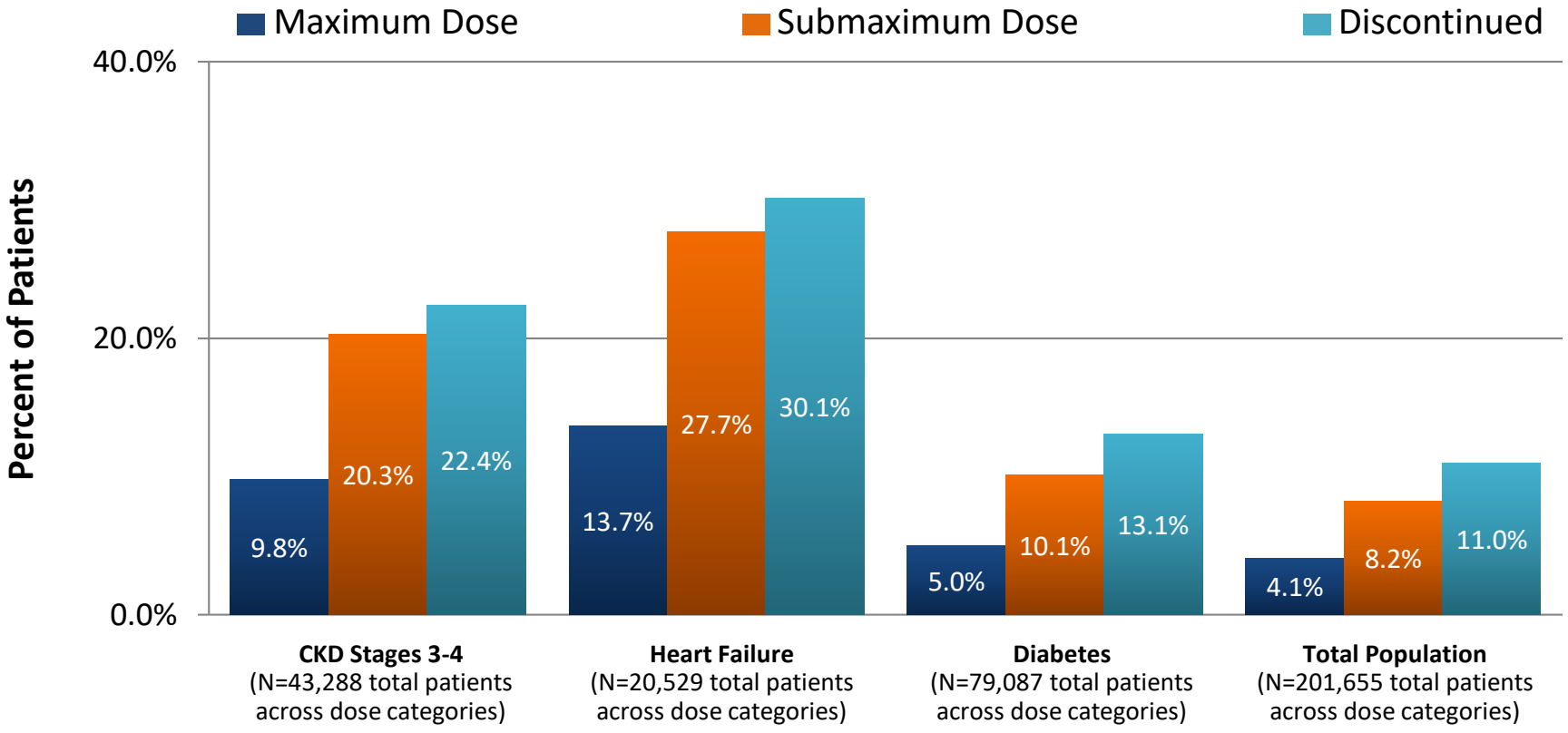
K^+: potassium; RAASi: renin-angiotensin-aldosterone system inhibitor

Yancy CW, et al., *Circulation*. 2016;134:[Epub ahead of print]. 2. Yancy CW, et al. *J iAm Coll Cardol*. 2017 Apr 21. pii: S0735-1097(17)37087-0. doi: 10.1016/j.jacc.2017.04.025. [Epub ahead of print].
3. Ponikowski P, et al. *Eur Heart J*. 2016 May 20. pii: ehw128. [Epub ahead of print] 4. Heart Failure Society of America, Lindenfeld J, et al. *J Card Fail*. 2010;16(6):475-539. 5. KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3(1). 6. National Institute for Health and Clinical Excellence (NICE) [UK]. Chronic kidney disease (partial update): early identification and management of chronic kidney disease in adults in primary and secondary care. 2014. https://www.nice.org.uk/guidance/cg182/evidence/update-full-guideline-191905165.
7. National Kidney Foundation. Guideline 11. http://www2.kidney.org/professionals/kdoqi/guidelines_bp/guide_11.htm. Accessed February 17, 2015. 8. Epstein M, et al. *Am J Manag Care*. 2015;21:S212-S220.

Percent Mortality by Prior RAASi Dose

Data from 205,108 patients from the Humedica data base indicate that

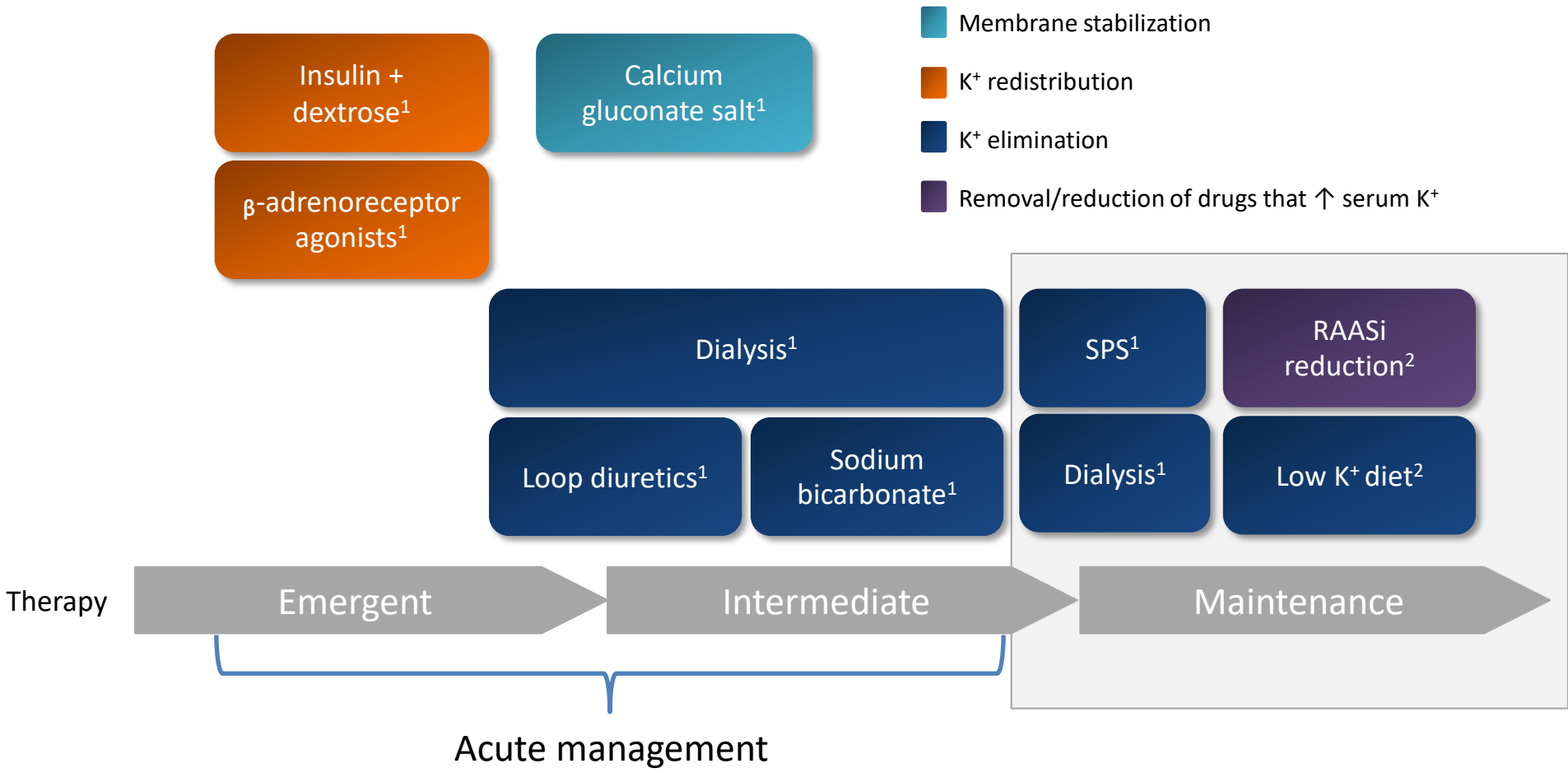
- *Few patients are prescribed maximum dose of RAASi (~20% across various comorbidities)*
- *HK associated with RAASi therapy was frequently followed by reduction in dosage or discontinuation of therapy*
- *Patients on maximum doses of RAASi therapies experienced fewer adverse outcomes compared with patients on submaximum doses or who discontinued RAAS inhibitors.*



RAASi: renin-angiotensin-aldosterone system inhibitor, HK: hyperkalemia.

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

Traditional Treatment Options for Hyperkalemia



K+: potassium; RAASi: renin-angiotensin-aldosterone system inhibitor, SPS: sodium polystyrene sulfonate.

1. Weisberg L. *Crit Care Med*. 2008;36(12):3246-3251. 2. Palmer BF, et al. *N Engl J Med.* 2004;351(6):585-592.

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Intermediate Management

- Dialysis can be used with poor kidney function
- Sodium bicarbonate can be used in CKD and metabolic acidosis
- Loop diuretics effective in excretion of potassium by the delivery of sodium in the collecting duct

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Maintenance

- Dietary Potassium intake restriction
- Lowering dose of drugs, administering every other day, or totally discontinuation is often needed
- Sodium polystyrene sulfonate- not well tolerated and may cause colonic necrosis and intestinal injury
- Potassium binding resins

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Overview of the Efficacy and Safety of Patiromer

In 2015, patiromer (Veltassa) was approved by the US Food and Drug Administration (FDA) for adults with hyperkalemia

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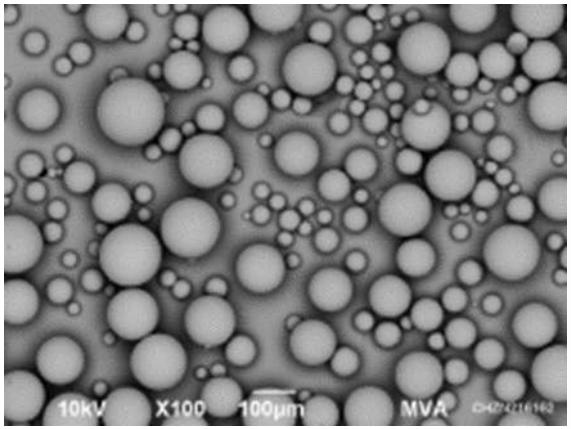
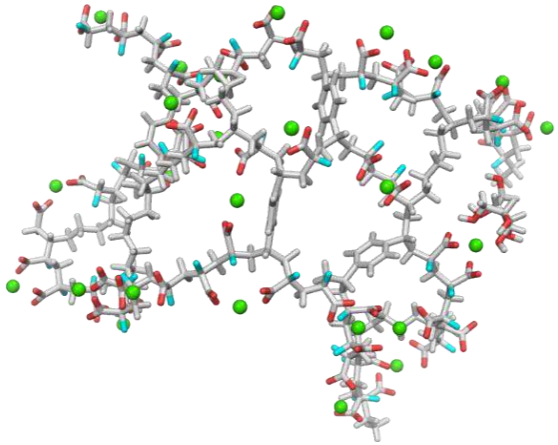
Patiromer:
A Non-absorbed Crosslinked Polymer

Electron Microscopy[1]



The crosslinked polymer forms 100-µm uniform spherical beads



Molecular structure of a polymer section (*green dots* represent calcium exchange ion)[2]

- Patiromer is a novel, non-absorbed polymer, designed to bind and remove K^+ from the GI tract[2]
  - Site of action is primarily in the colon, where K^+ is the most abundant cation and where residence time of the polymer is the longest
- Ca^{2+} was purposely selected as the exchange ion. Ca^{2+} exchange avoids issues such as increased Na^+ load, which has been seen with SPS[3]

Ca^{2+}: calcium; GI: gastrointestinal; K^+: potassium; Na^+: sodium; SPS: sodium polystyrene sulfonate

1. Bushinsky DA, et al. Poster presented at: ASN Kidney Week 2014; Philadelphia, PA; November 11-16, 2014; Poster SA-PO153. 2. Buysse JM. Hyperkalemia: physiology, control, and potassium binder mechanism of action. Presented at: 8th Global Cardiovascular Clinical Trialists Forum; Paris, France; December 2-3, 201[illegible]
3. Data on file. Redwood City, CA: Relypsa, Inc.

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Patiromer Is Designed to Bind Potassium Predominantly in the Colon

- Patiromer travels through the GI tract over 24-72 hours[1,2]
  - Patiromer is fully ionized at the physiologic pH of the colon for optimal ion exchange[3]
  - Carboxylate groups of patiromer bind to K^+, which is primarily in the colon due to upregulation of BK channels in colonic epithelial cells[3]
  - Patiromer beads are excreted, leading to removal of excess K^+ and reduction of serum K^+ levels[3]

BK: big K^+; GI: gastrointestinal; K^+: potassium.

1. Data on file. Redwood City, CA: Relypsa, Inc.
2. Jung HK, et al., Yonsei Med J. 2003;44(2):265-272.
3. Li L, et al. *J Cardiovasc Phamacol Ther.* 2016;21(5):456-465.

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Dosing

- Starting dose 8.4g per day
- Titration- At weekly intervals: can be increased or decreased by **8.4 g/day** up to a maximum of **25.2 g/day**
- Dosing strengths**:** 8.4 g/day, 16.8 g/day, 25.2 g/day + 1/3 cup of water

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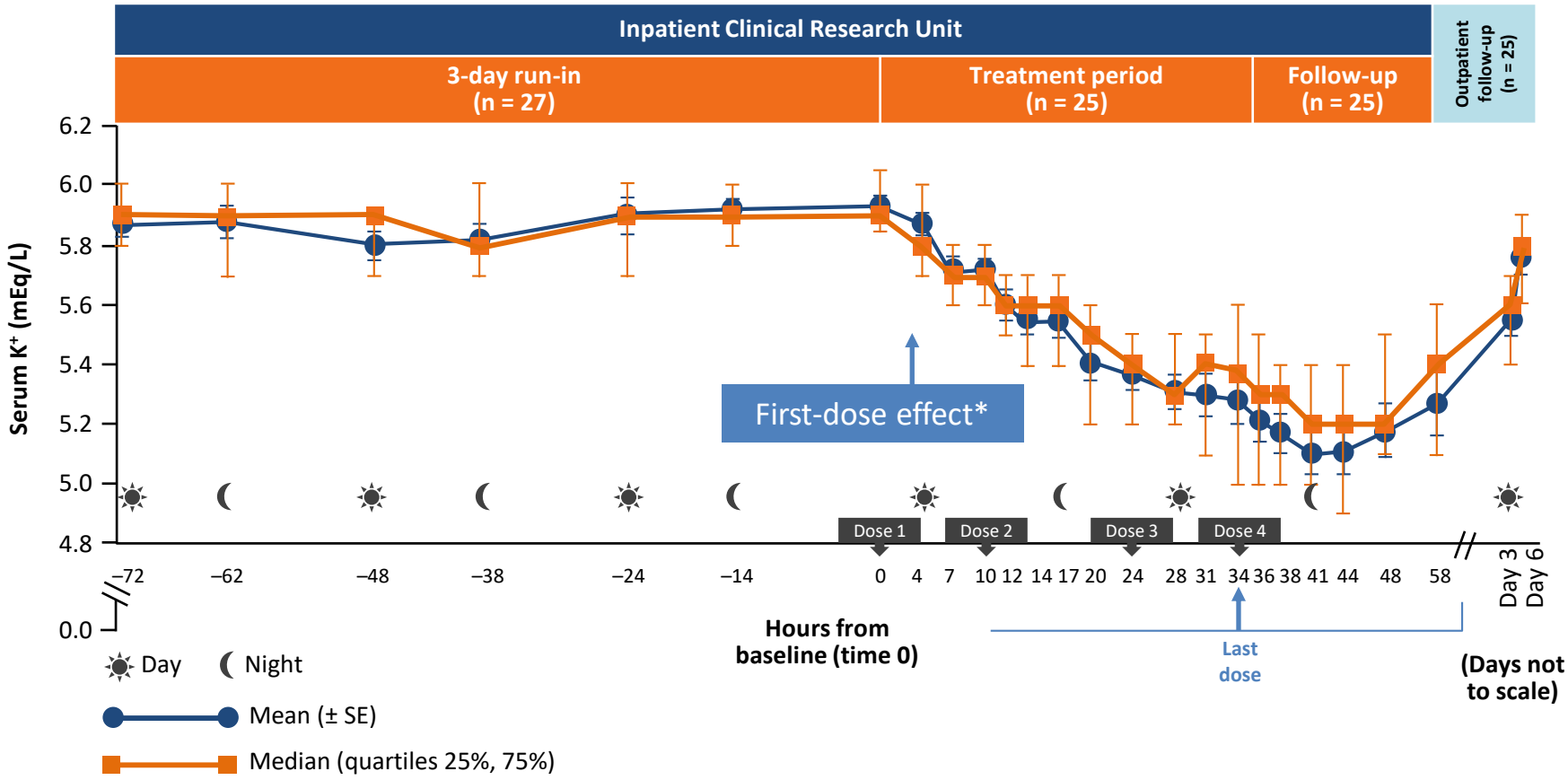
Onset of Action Study: Primary Endpoint (Change in Serum K^+, Observed Serum K^+ [mEq/L] Over Time)



Significant reductions occurred at all assessments from 7 to 48 hours ($p \leq 0.004$ at 7 and 10 hours; $p < 0.001$ for 12 to 48 hours)

*Earliest timepoint where mean change from baseline in serum K^+ was significant; significant reduction seen at 7 hours (before the second patiromer dose).
Data presented as median (quartiles 25%,75%), mean (SE).

K^+: potassium; SE: standard error.

From Bushinsky DA, et al. Published online ahead of print September 16, 2015. *Kidney Int.* doi: 10.1038/ki.2015.270,

Key Clinical Studies

- OPAL-HK[1]
  - Phase 3 study
- AMETHYST-DN[2]
  - Phase 2, dose-finding, 1-year safety study

1. Weir M, et al. *N Engl J Med*. 2015;372(3):211-221.
2. Bakris G, et al. *JAMA* 2015; 314(2):151-161.

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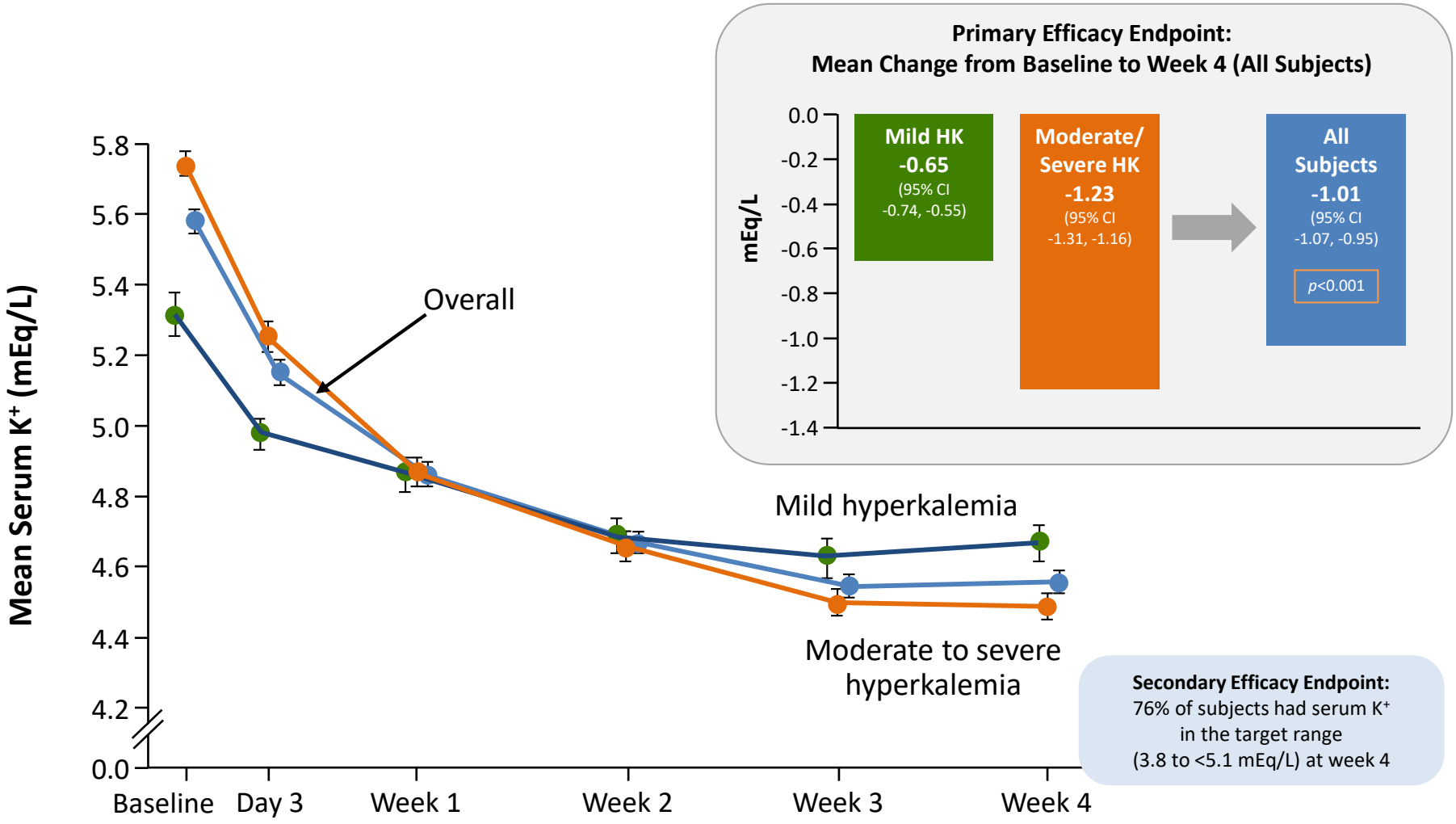
Populations Studied in Patiromer Clinical Trials

- Efficacy and safety of patiromer were evaluated in a population of subjects with advanced CKD with or without heart failure who were receiving RAASi medications[1-3]
- Characteristics of the pooled study population included[1]
  - 100% receiving RAASi
  - 60% >65 years of age (20% ≥75 years)
  - 88% had ≥ stage 3 CKD (29% had stage 4 CKD)
  - 49% had heart failure
  - 97% had hypertension
  - 73% had diabetes
  - Wide range of severity of hyperkalemia (serum K^+ 5.1 to <6.5 mEq/L)
    - 28% of subjects had a serum K^+ ≥5.5-<6.0 mEq/L at baseline
    - 8% of subjects had a serum K^+ ≥6.0 mEq/L at baseline

CKD: chronic kidney disease; K^+: potassium; RAASi: renin-angiotensin-aldosterone system inhibitor.

1. Data on file. Relypsa, Inc. Redwood City, CA.
2. Weir MR, et al. *N Engl J Med.* 2015;372(3):211-221.
3. Bakris G, et al. Poster presented at: ASN Kidney Week 2014; Philadelphia, PA; November 11-16, 2014; Poster SA-PO1099.

OPAL HK (Phase 3 Part A): Primary and Secondary Efficacy Endpoints

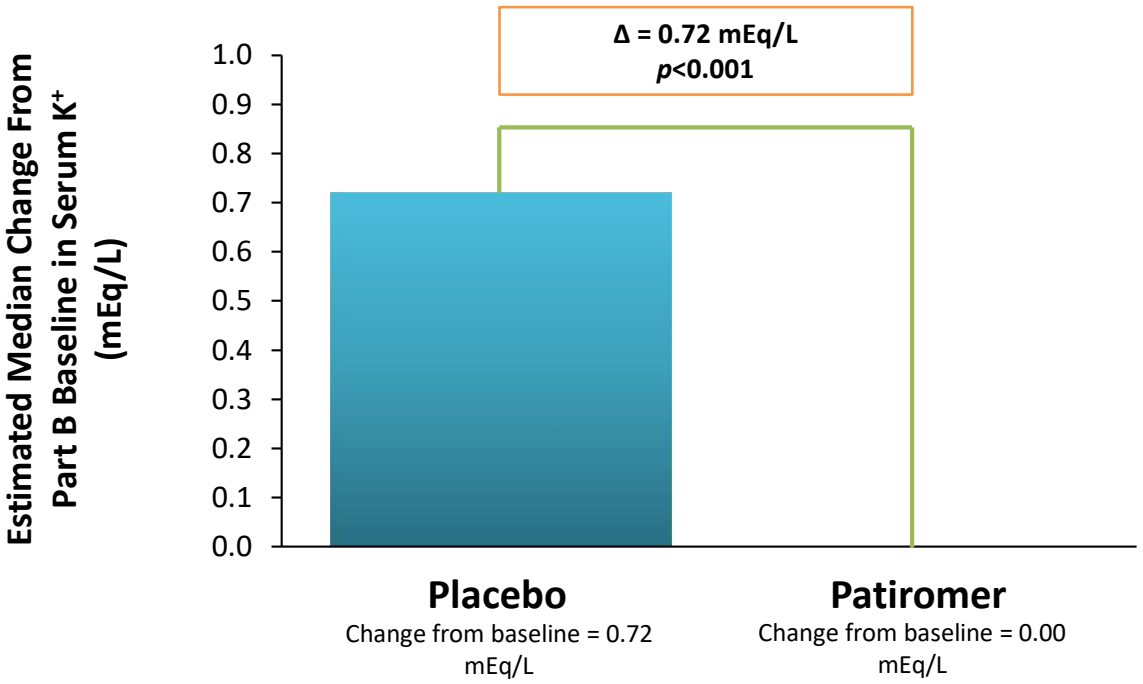


CI: confidence interval; HK: hyperkalemia; K^+: potassium.

Weir MR, et al. *N Engl J Med.* 2015;372(3):211-221.

OPAL HK (Phase 3 Part B): Primary Efficacy Endpoint

Part B Primary Efficacy Endpoint:
difference between groups in the median change in serum K^+ from Part B baseline to Part B week 4*



*Or earlier time point if subject first had serum K^+ <3.8 mEq/L or ≥5.5 mEq/L.

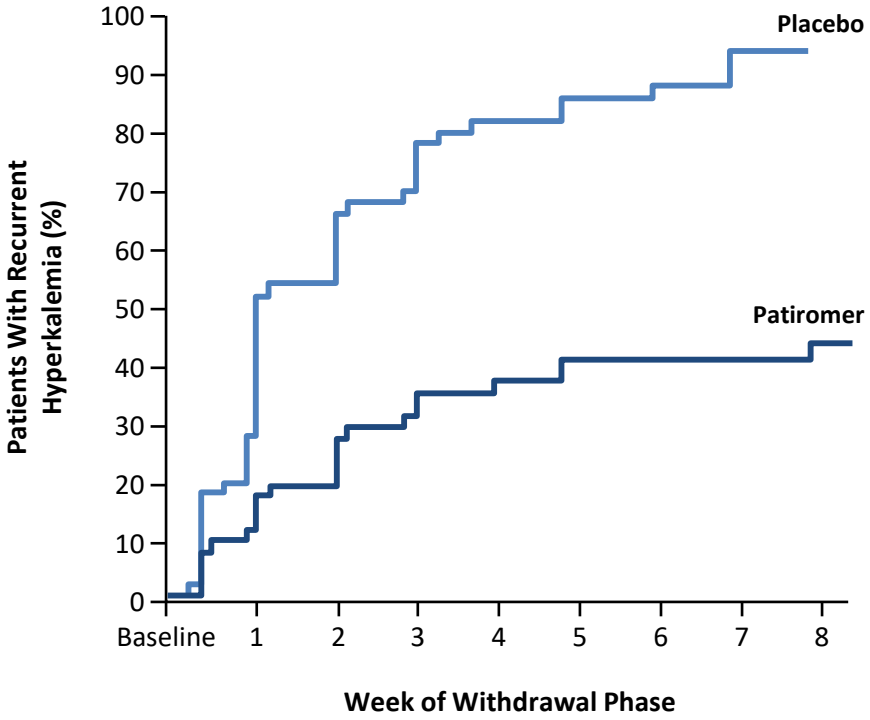
K^+: potassium.

Weir MR, et al. *N Engl J Med.* 2015;372(3):211-221.

OPAL HK (Phase 3 Part B): Secondary Efficacy Endpoint

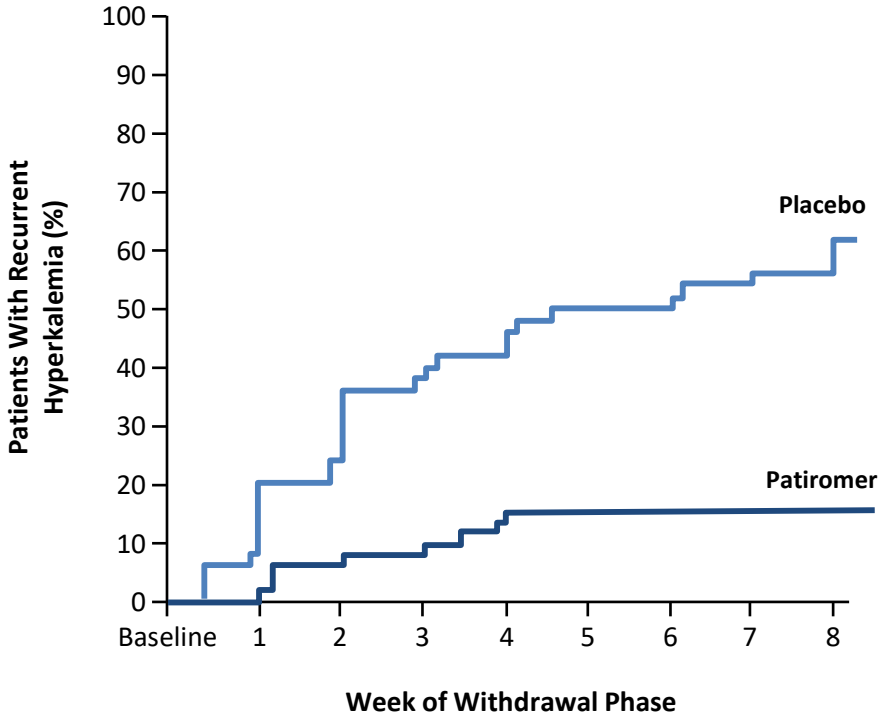
Time to First Recurrent Hyperkalemia Event

Time to First Serum K^+ Level ≥5.1 mEq/L



No. at Risk									
Placebo	52	37	24	16	10	8	8	7	1
Patiromer	55	47	42	36	34	30	29	29	23

Time to First Serum K^+ Level ≥5.5 mEq/L



No. at Risk									
Placebo	52	46	38	31	29	25	25	23	15
Patiromer	55	53	49	48	45	43	42	42	32

K^+: potassium.

From *N Engl J Med,* Weir MR, et al, Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors, 372(3):211-221. Copyright © 2015 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Important Safety information and Adverse Events

Indications and Usage and Restrictions

Indications and Usage

- VELTASSA® (patiromer) is indicated for the treatment of hyperkalemia
- Limitations of Use
  - VELTASSA should not be used as an emergency treatment for life-threatening hyperkalemia because of its delayed onset of action.

Contraindications

- Patients with a history of a hypersensitivity reaction to VELTASSA or any of its components

There are no restrictions regarding concomitant use of VELTASSA with immediate-acting emergency treatments for hyperkalemia

VELTASSA [package insert]. Redwood City, CA. Relypsa, Inc. May 2018.

VELTASSA® (patiromer) Warnings and Precautions

Worsening of Gastrointestinal Motility

- VELTASSA should be avoided in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders, because VELTASSA may be ineffective and may worsen gastrointestinal conditions
- Patients with a history of bowel obstruction or major gastrointestinal surgery, severe gastrointestinal disorders, or swallowing disorders were not included in clinical studies

Hypomagnesemia

- In clinical studies, hypomagnesemia was reported as an adverse reaction in 5.3% of patients treated with VELTASSA
  - VELTASSA binds to magnesium in the colon, which can lead to hypomagnesemia
  - Approximately 9% of patients in clinical trials developed hypomagnesemia with a serum magnesium value <1.4 mg/dL
- Monitor serum magnesium and consider magnesium supplementation in patients who develop low serum magnesium levels on VELTASSA

VELTASSA [package insert]. Redwood City, CA. Relypsa, Inc. May 2018.

Clinical Studies: Pooled Safety Population

- **Adverse reactions reported in ≥2% of patients**
- Most adverse reactions were mild to moderate across studies up to 1 year

Adverse Reactions in Patients Treated With VELTASSA® (patiromer) (N=666)*	
Constipation	7.2%
Hypomagnesemia	5.3%
Diarrhea	4.8%
Nausea	2.3%
Abdominal discomfort	2.0%
Flatulence	2.0%

Mild to moderate hypersensitivity reactions

- Reported in 0.3% of patients treated with VELTASSA in clinical trials
- Reactions have included edema of the lips

Discontinuation due to adverse reactions

- 2.7% of patients discontinued due to GI reactions
- GI reactions included vomiting, diarrhea, constipation, and flatulence

*The dosage and duration of study treatment (4 to 52 weeks) and follow-up (1 to 4 weeks post treatment) differed across the 4 studies pooled in this analysis.

GI: gastrointestinal.

VELTASSA [package insert]. Redwood City, CA. Relypsa, Inc. May 2018.

Overview of the Efficacy and Safety of Sodium Zirconium Cyclosilicate

In 2018, ZS-9 (Lokelma) became FDA approved for adults with hyperkalemia

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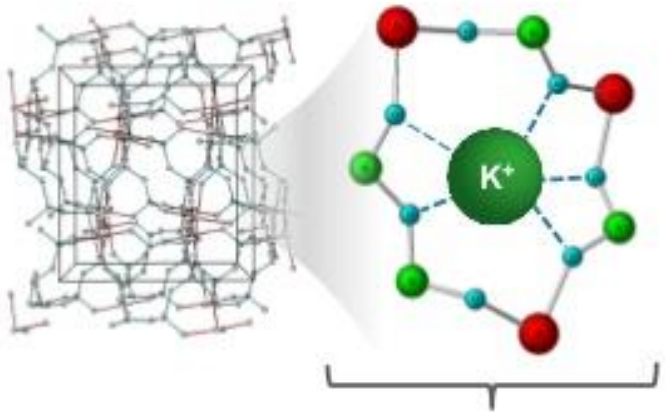
Sodium Zirconium Cyclosilicate (ZS-9) is a Selective K+ Ion Trap

ZS-9 Crystal Structure



ZS-9 PROPERTIES

- Unique microporous zirconium silicate compound
- Designed with tiny (only 3Å in diameter) pore size to selectively trap K^+ in the GI tract in exchange for hydrogen and sodium
- Insoluble and does not swell on contact with water
- Not systemically absorbed

Abbreviations: GI, gastrointestinal

*Stavros et al., PLOSONE, 2015

About Sodium Zirconium Cyclosilicate

- Potassium lowering action is based on size selective micropores in the zirconium silicate crystal structure.
- The pores trap K^+ ions in intestinal tract in exchange for protons(H^+) and sodium(Na^+).
- Potassium binding ability is 9 times that of organic polymer resins.
- Potassium binding of ZS-9 is more selective by a factor of > 125 for potassium over calcium.
- Zs-9 is insoluble ,does not swell on contact with water, and is not absorbed systemically.#
- Binding to K^+ is throughout the intestinal tract.@

Dosing

The recommended starting dose: 10g, administered three times daily. Once normal potassium levels in the blood has been achieved, a maintenance dose of 5g once daily is recommended with possible titration up to 10g daily or down to 5g once every other day to maintain a normal potassium level

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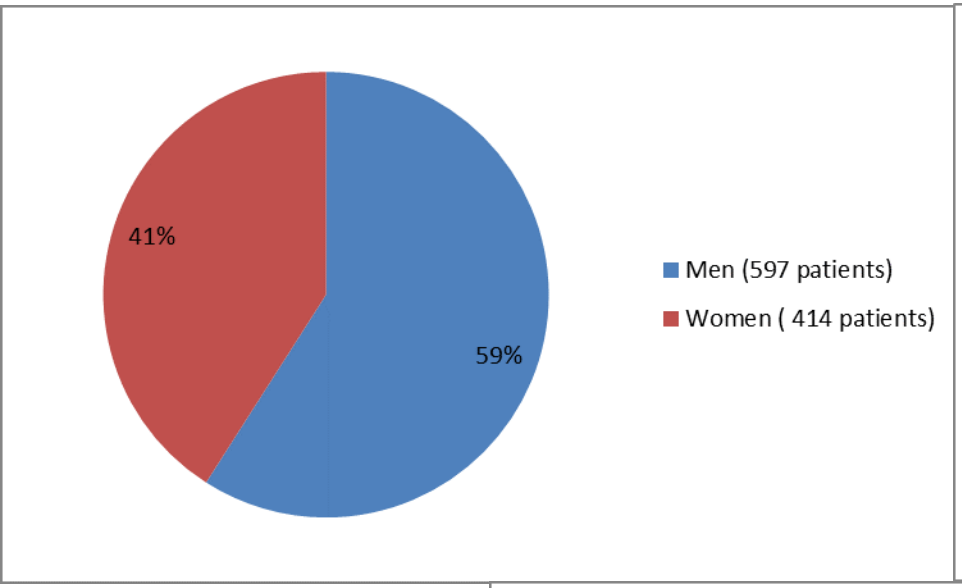
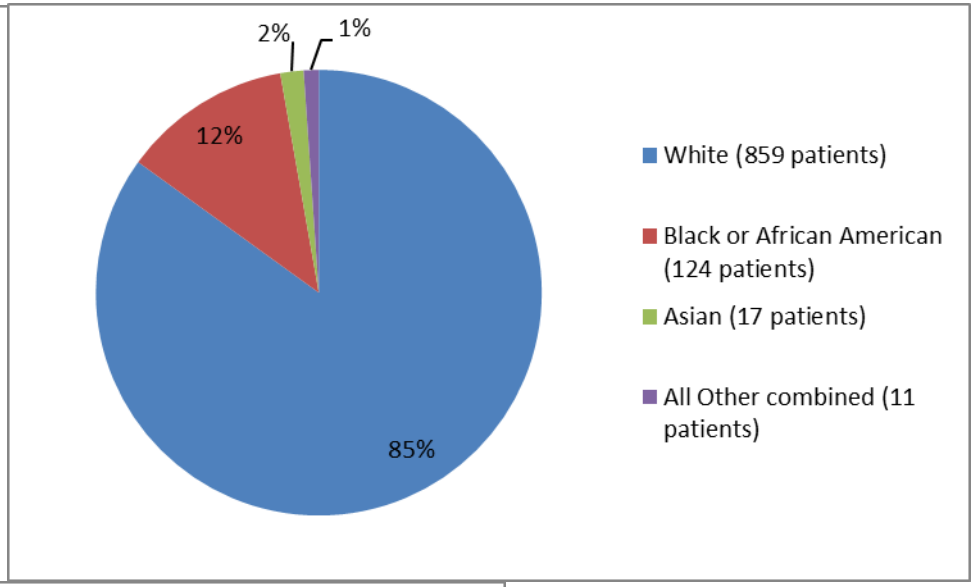
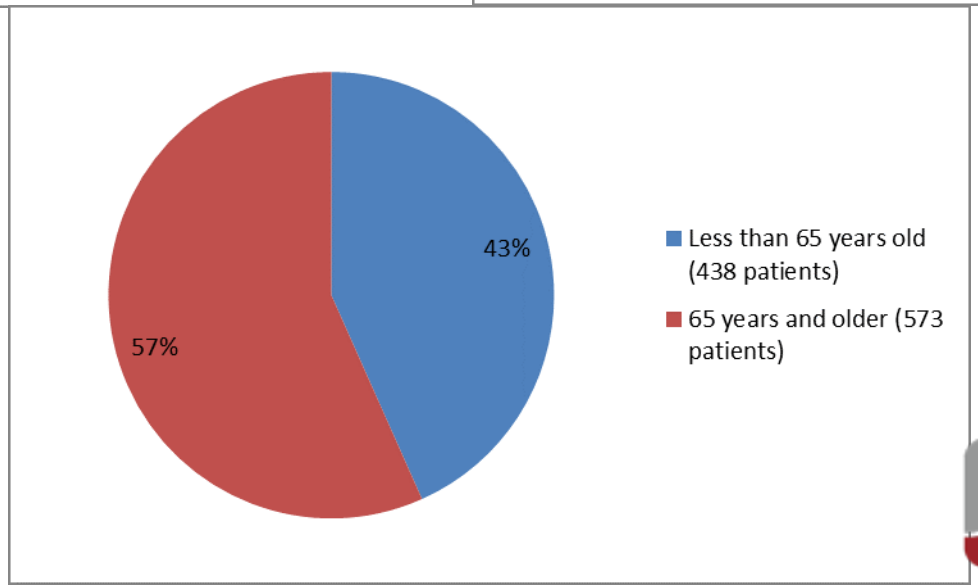
2 Clinical Trials approved by FDA







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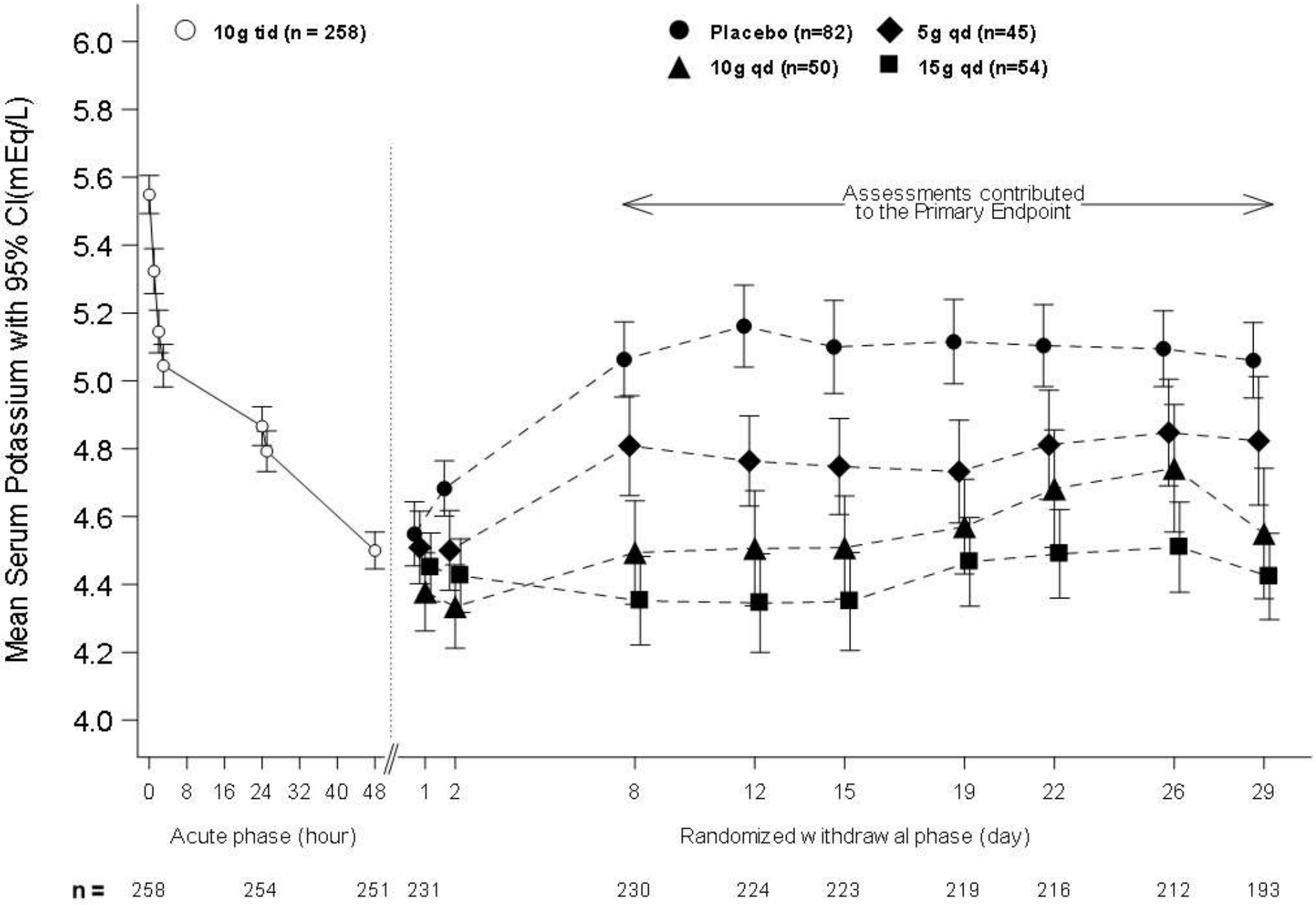
10g tid (n = 258)
Placebo (n=82)
5g qd (n=45)
10g qd (n=50)
15g qd (n=54)
Assessments contributed to the Primary Endpoint
Mean Serum Potassium with 95% CI(mEq/L)
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
0 8 16 24 32 40 48
1 2
8 12 15 19 22 26 29
Acute phase (hour)
Randomized withdrawal phase (day)
n = 258 254 251 231 230 224 223 219 216 212 193

Lokelma (ZS-9) Warnings and Precautions

Worsening of Gastrointestinal Motility

- Avoid LOKELMA in patients with severe constipation, bowel obstruction or impaction, including abnormal post-operative bowel motility disorders.
- LOKELMA has not been studied in patients with these conditions and it may be ineffective and may worsen gastrointestinal conditions

Edema

- Each 5 g dose of LOKELMA contains approximately 400 mg of sodium. In clinical trials of LOKELMA, edema was generally mild to moderate in severity and was more commonly seen in patients treated with 15 g once daily. Monitor for signs of edema, particularly in patients who should restrict their sodium intake or are prone to fluid overload (eg., heart failure or renal disease). Advise patients to adjust dietary sodium, if appropriate. Increase the dose of diuretics as needed

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Case Study #1

- John is a 74 year old male with medical history of DM, HTN, HFrEF, GERD, and Hypothyroid. Medications: Metoprolol XL 25mg daily, Lasix 40mg daily, Entresto 24/26mg BID, Spironolactone 12.5mg daily, Metformin 500mg BID, Levothyroxine 50mcg daily, and Ranitidine 75mg BID. Follows with Cardiology q6months. Baseline labs: K 4.4, BUN 10, Cr 1.1, Na 136. BP 112/60, HR 66, Weight 176lbs

Case Study #1

- John develops fever 104 degree F, HR 104 bpm, BP 80/50, malaise and body aches. He is evaluated in the ED and diagnosed with Influenza A. Admission labs: K 6.5, BUN 66, Cr 2.3, Na 129. EKG- sinus tachycardia, Tall, peaked T waves with a narrow base.

- What is the first intervention?
- A. IV fluids
- B. Tamiflu 75mg BID x5 days
- C. Insulin 10 units with 2 amps of D50W
- Dialysis

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Case Study #2

- John improves and discharges from hospital after 7 days. Cardiology follow up in 1 month: BP 110/70, HR 68, Weight 172lbs, routine labs: K 5.9, BUN 23, Cr 2.1, Na 133. EKG: NSR Cardiology discontinued Spironolactone and decreased Lasix 20mg daily. Repeat labs: BUN 18, Cr 1.9, K 5.5, Na 133, Weight 177lbs euvolemic on clinical exam

- What is the next intervention?
  A. ZS-9 5g daily or Patiromer 8.4g daily
  B. Kayexalate 30g po x1
  C. Increase Lasix 40mg daily x3 days
  D. Continue to monitor

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Take away

- The treatment of acute hyperkalemia is well recognized. Equally important to develop treatments for chronic use, require long term data for the safety of these compounds- clinical outcomes and quality of life data
- Discussion about noncompliance and abrupt discontinuation of therapy by patients and risk of rebound hyperkalemia needs to be educated to patients taking ZS-9 and Patiromer
- Cost
- Shared Decision making with patient and provider

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