In-Hospital Heart Failure Management

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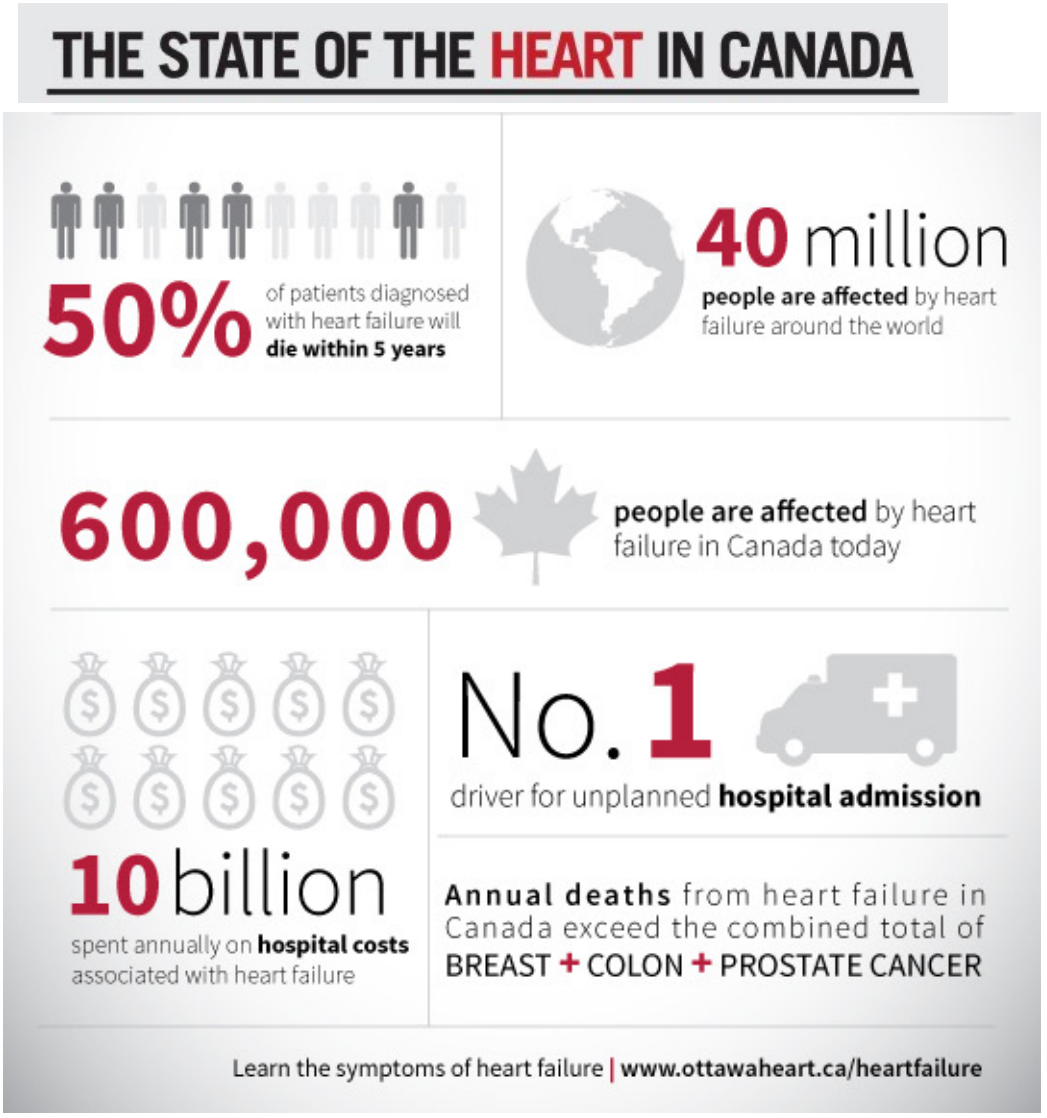
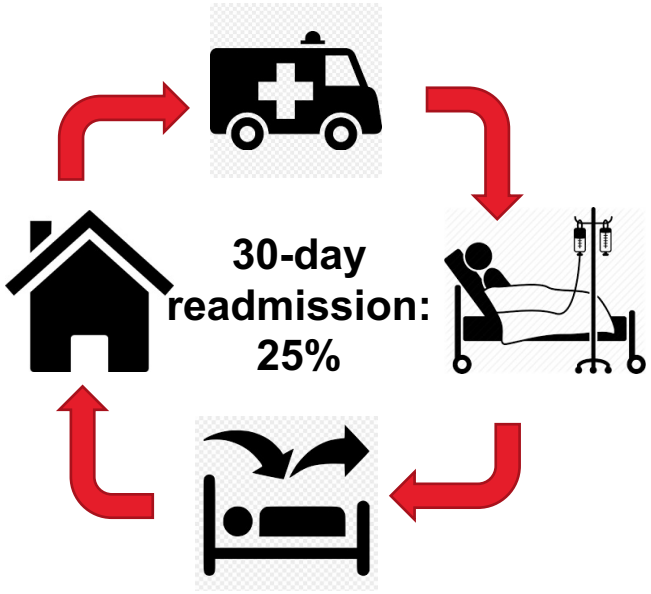
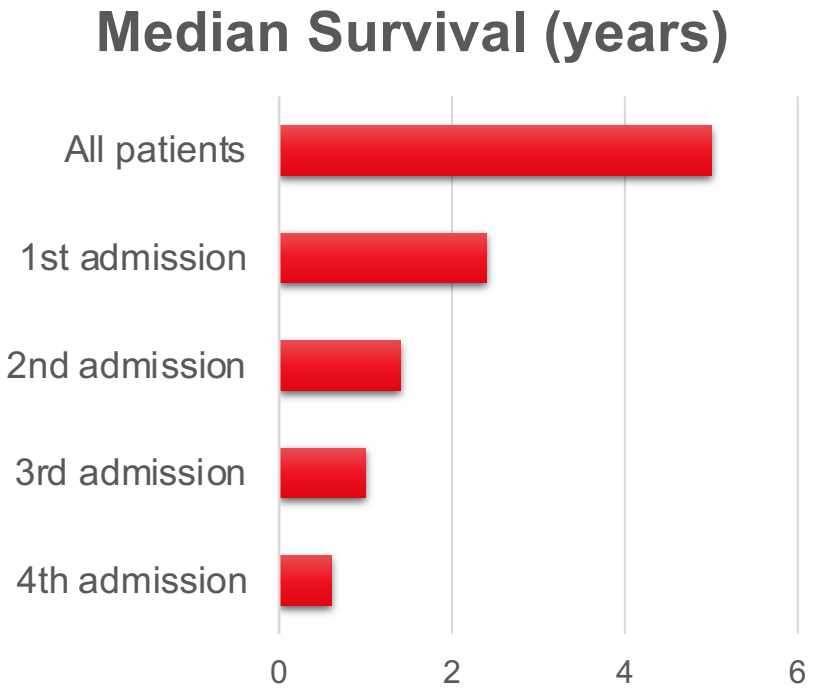
Conflict of Interest Disclosures

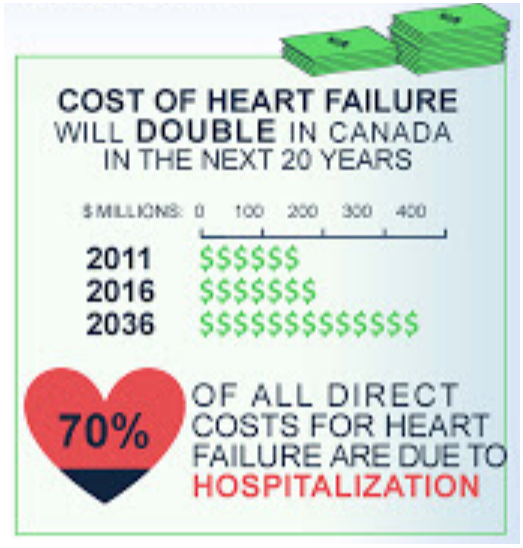
- **Speaking fees / Consulting fees**: Servier, Novartis, Janssen, Astra Zeneca, Boehringer Ingelheim, Bayer

Heart Failure Hospitalization in Canada





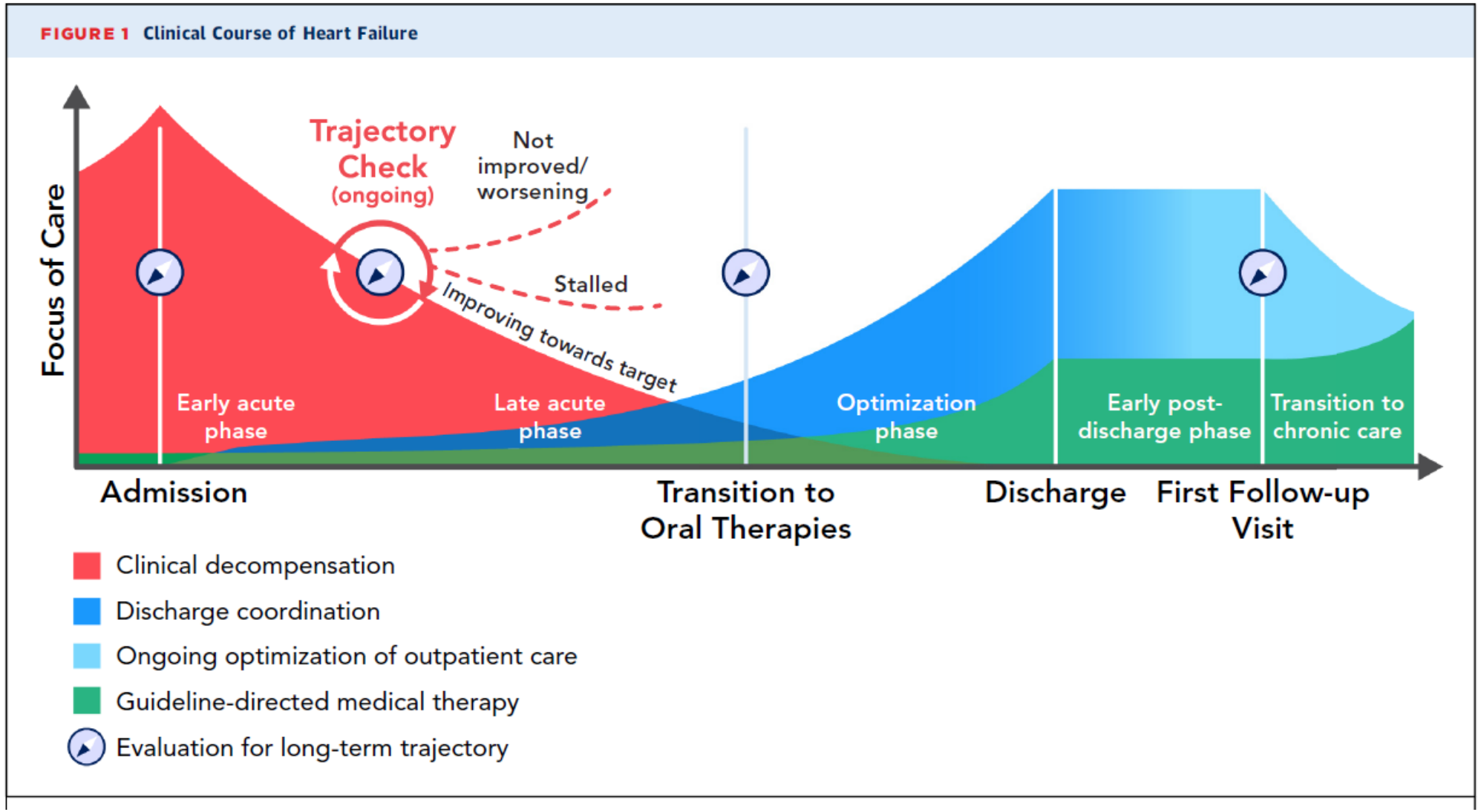




- In-Hospital Optimization
- Goal Directed Medical Therapy
- Remote Monitoring Technology
- Adequate Care Transitions

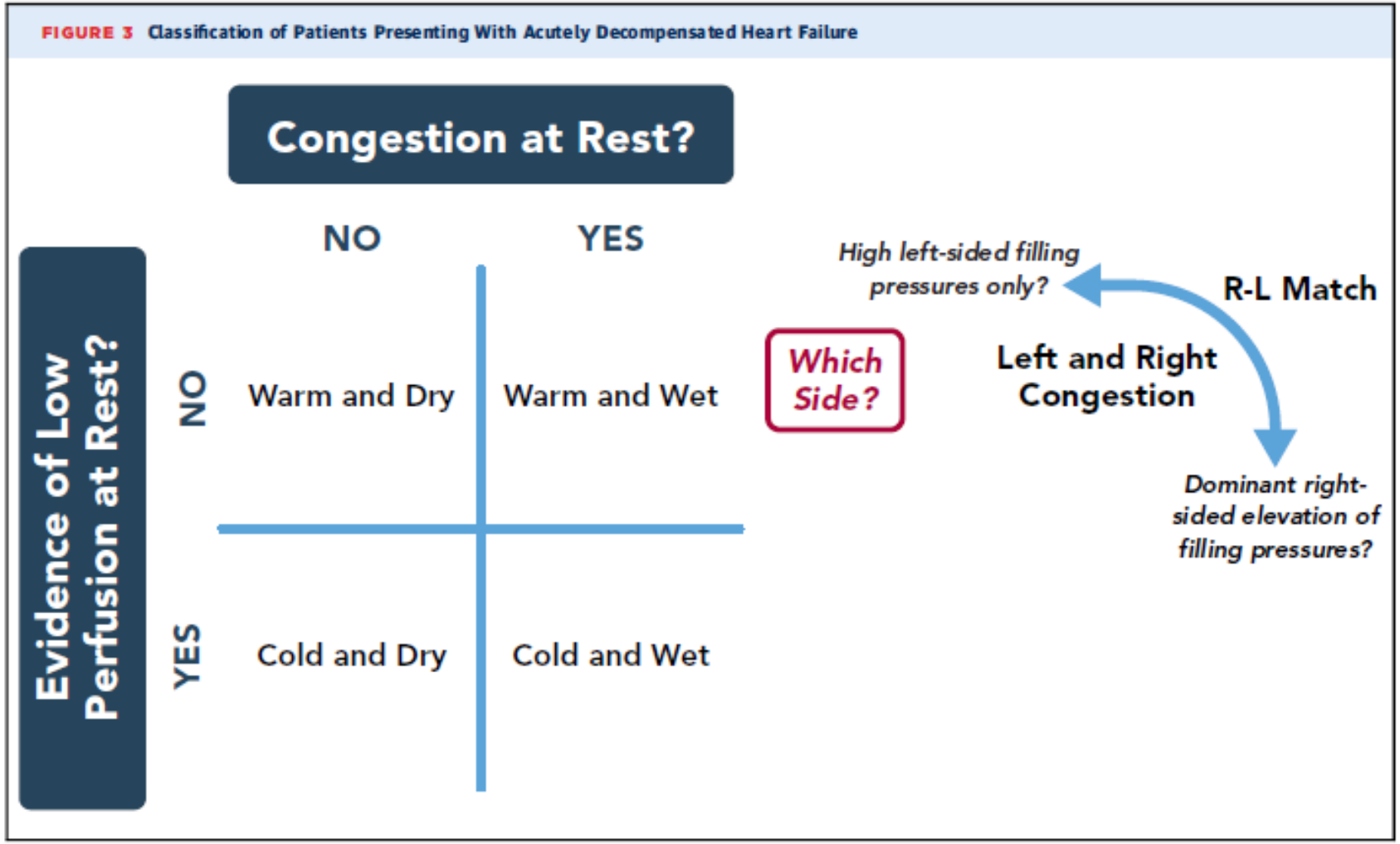
Go et al. *Circulation* 2013; 127: e6–e245.

Phase Based Approach to Acute Heart Failure Management



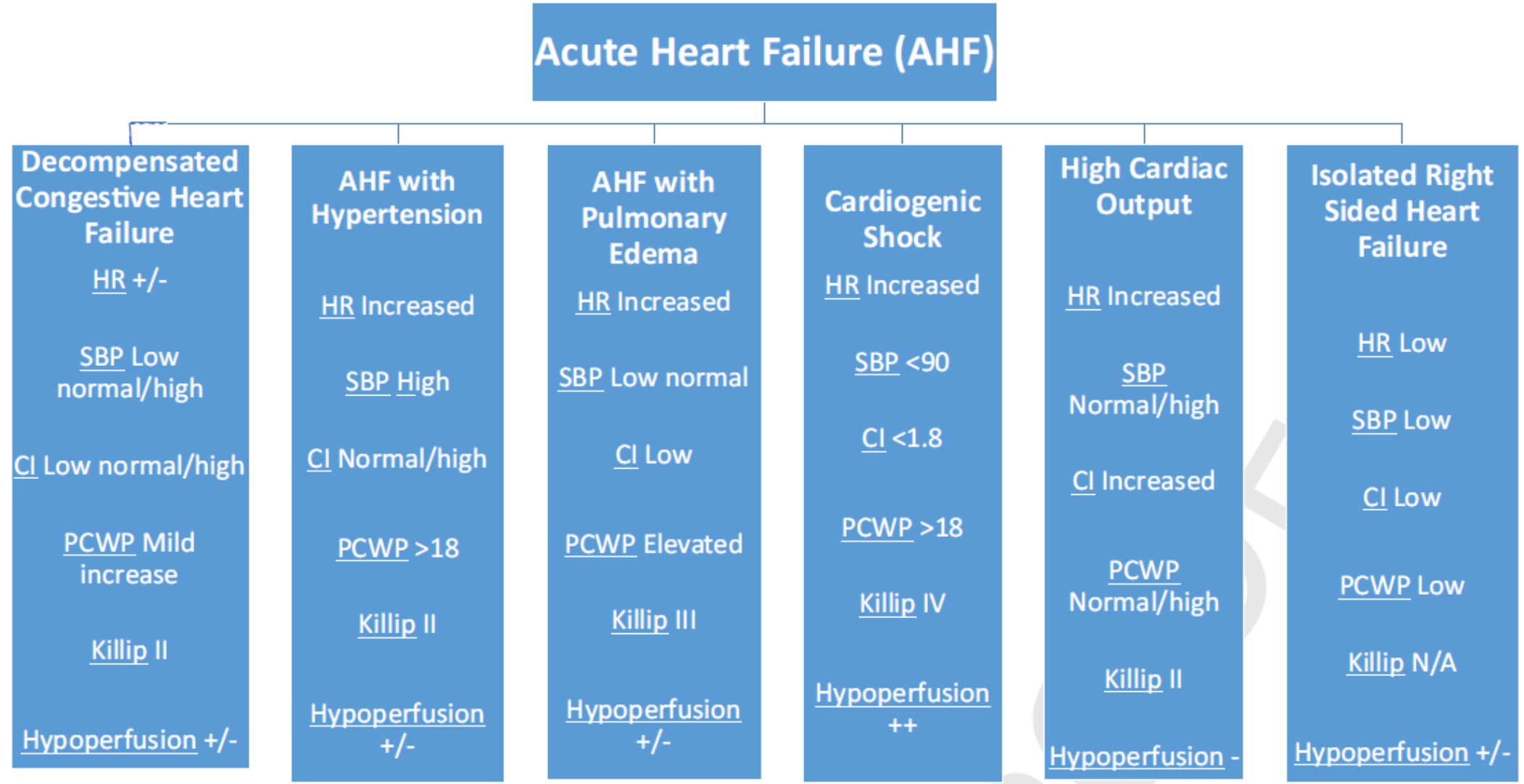
Hollenberg SM, JACC 2019; 74915):1966

Initial Evaluation of the Patient with Decompensated Heart Failure



Hollenberg SM, JACC 2019; 74915):1966

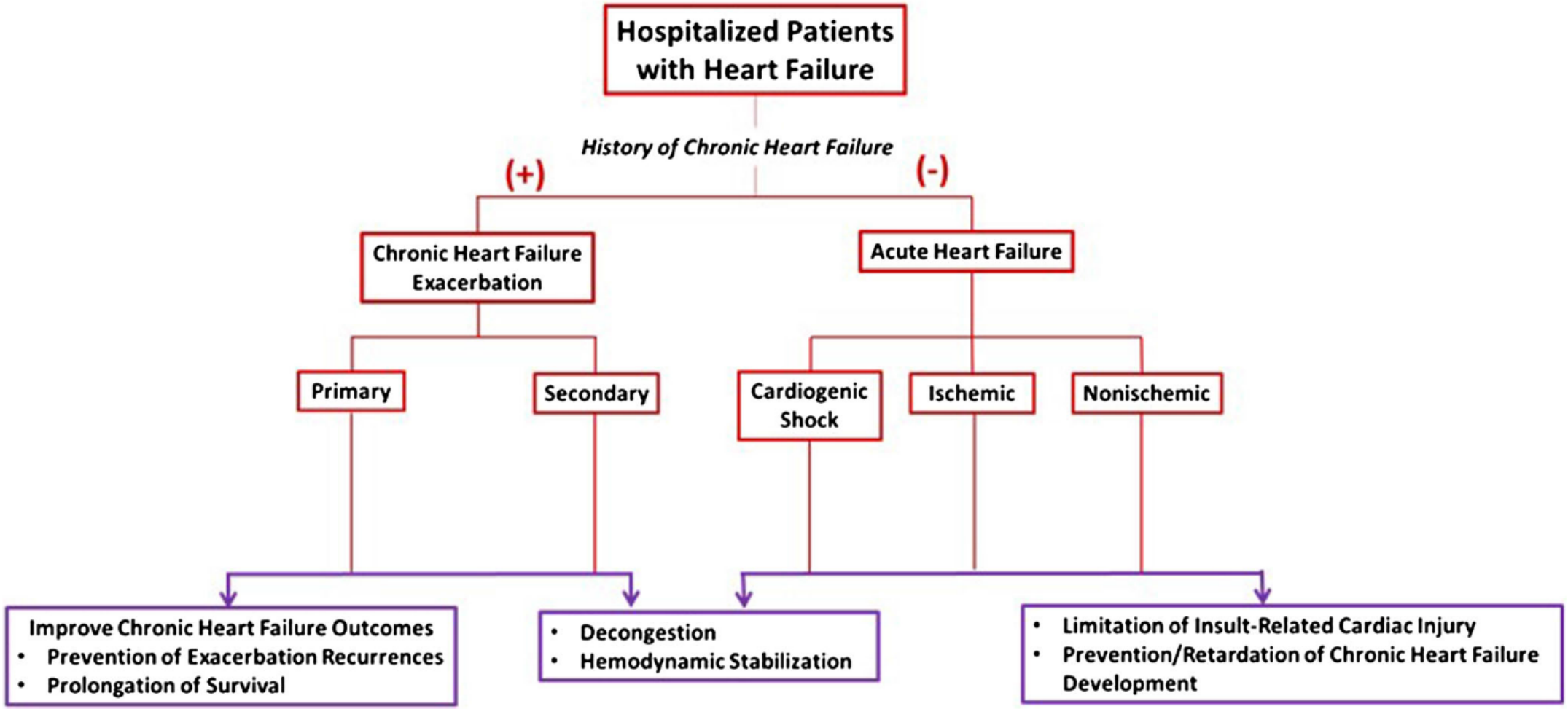
Initial Evaluation of the Patient with Decompensated Heart Failure



HR = Heart Rate, SBP = Systolic Blood Pressure (mmHg), CI = Cardiac Index (L/min/m2), PCWP = Pulmonary Capillary Wedge Pressure (mmHg), Kilip = Killip Classification

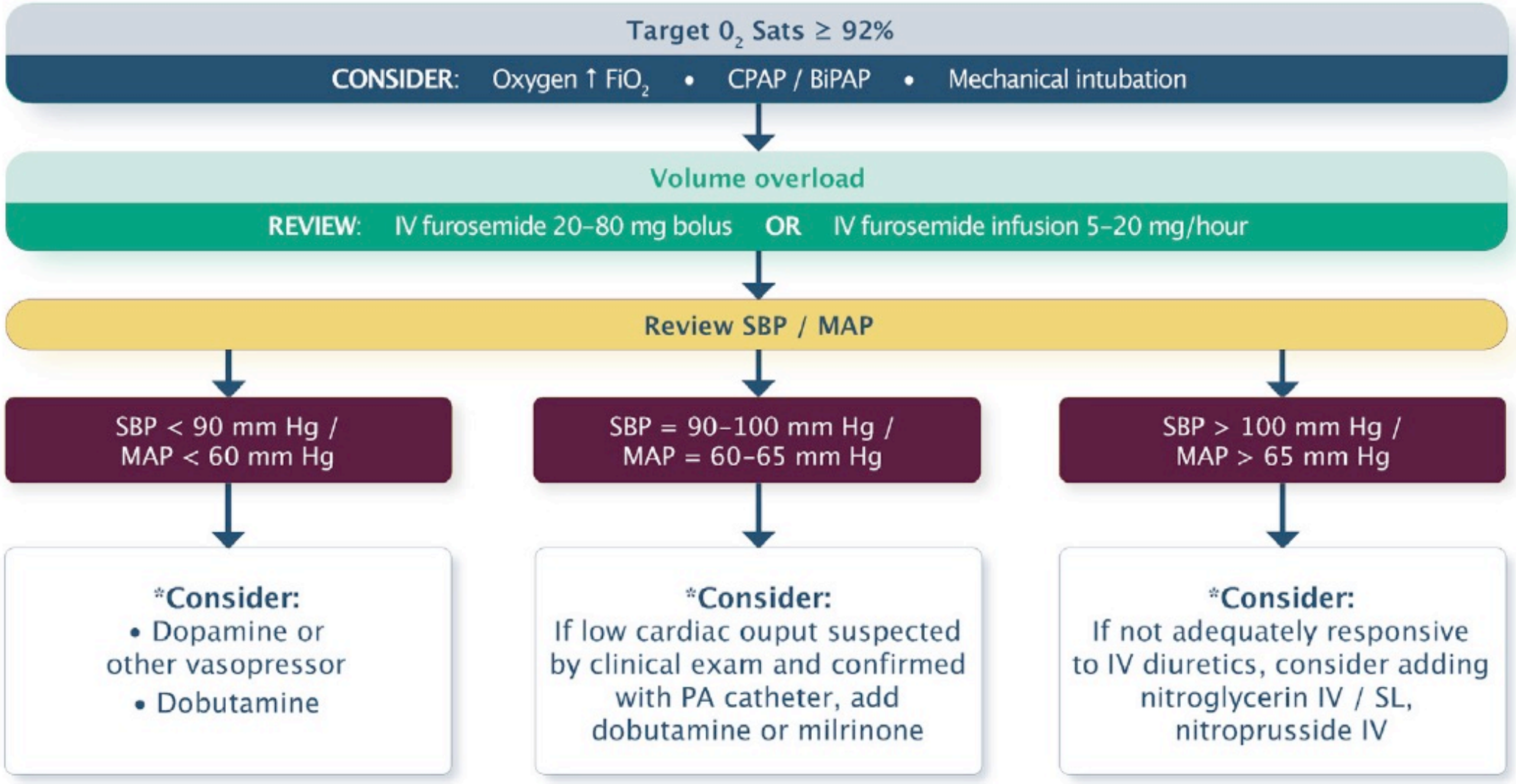
Gupta; Can J Cardiol 2021, in press

Initial Evaluation of the Patient with Decompensated Heart Failure



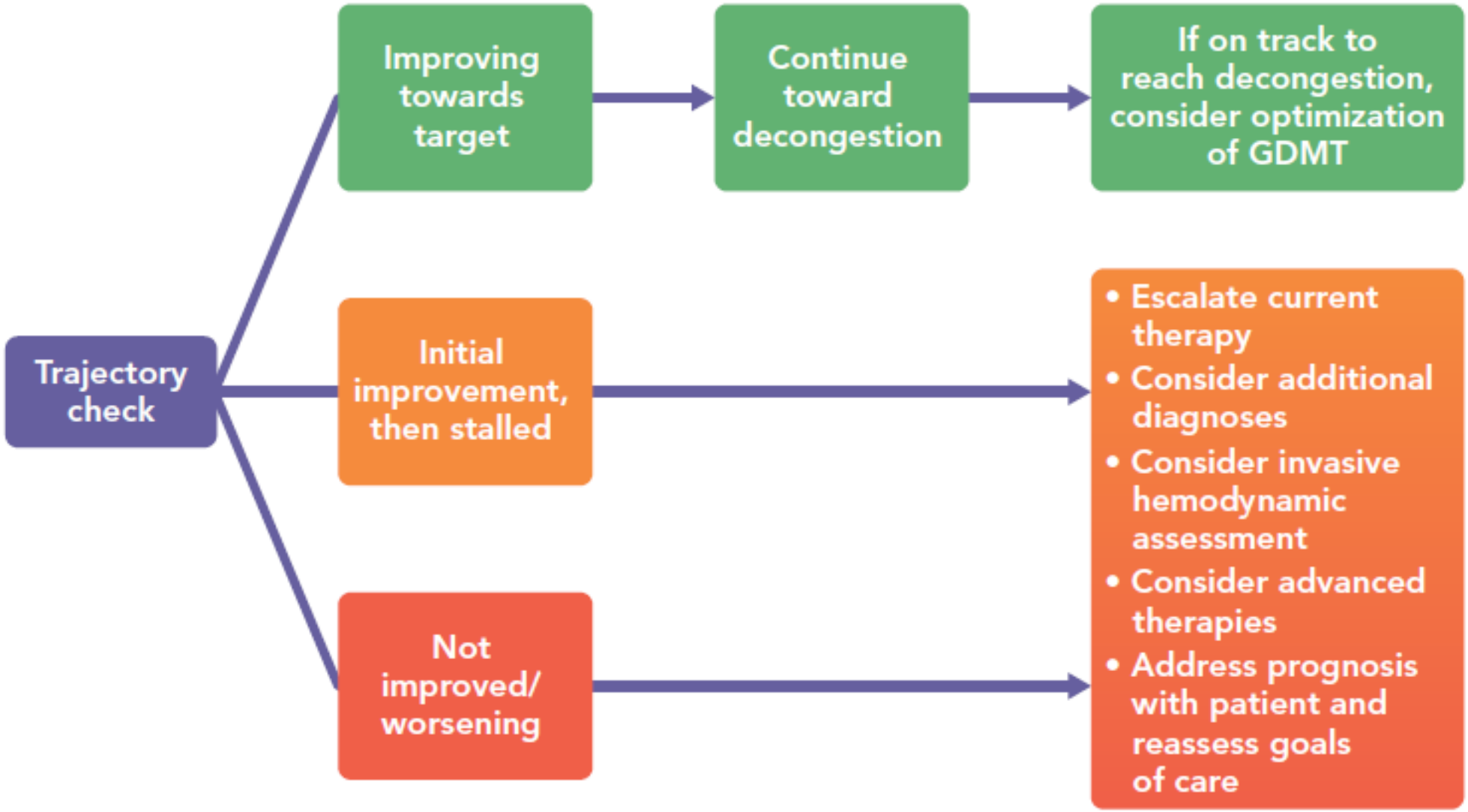
Xanthopoulos, Heart Failure Rev 2020: 25:907

(Over) Simplified Approach to Acute Heart Failure Management



Ezekowitz, Can J Cardiol 2017:1342-1433

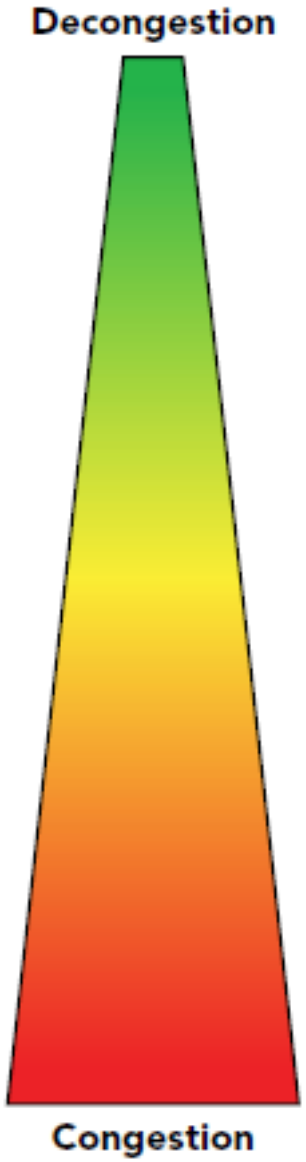
Clinical Trajectories and Their Implications for Therapy



Hollenberg SM, JACC 2019; 74915):1966


EVIDENCE BASED
THERAPIES FOR
ACUTE HEART
FAILURE

Diuretic Therapy Almost Always Essential Part of Stabilization



Freedom from clinical congestion

No peripheral edema

No rales

No dyspnea on minimal exertion

No hepatomegaly or congestive GI symptoms

No orthopnea or bendopnea

Jugular venous pressure ≤6-8 mm Hg

No hepatojugular reflex

Common reasons for Residual Congestion

Low cardiac output state
Dominant right heart failure
Advanced renal disease
Symptomatic hypotension
Limitations to patient engagement in self-care

Lack of improvement in signs/symptoms of HF

Lack of decrease in natriuretic peptide levels

Lack of decrease in weight

IV Diuretics

Initiate IV loop diuretics early (ER or immediately after admission)

Initial dose usually 1-2.5 times total daily oral loop diuretic in furosemide equivalents

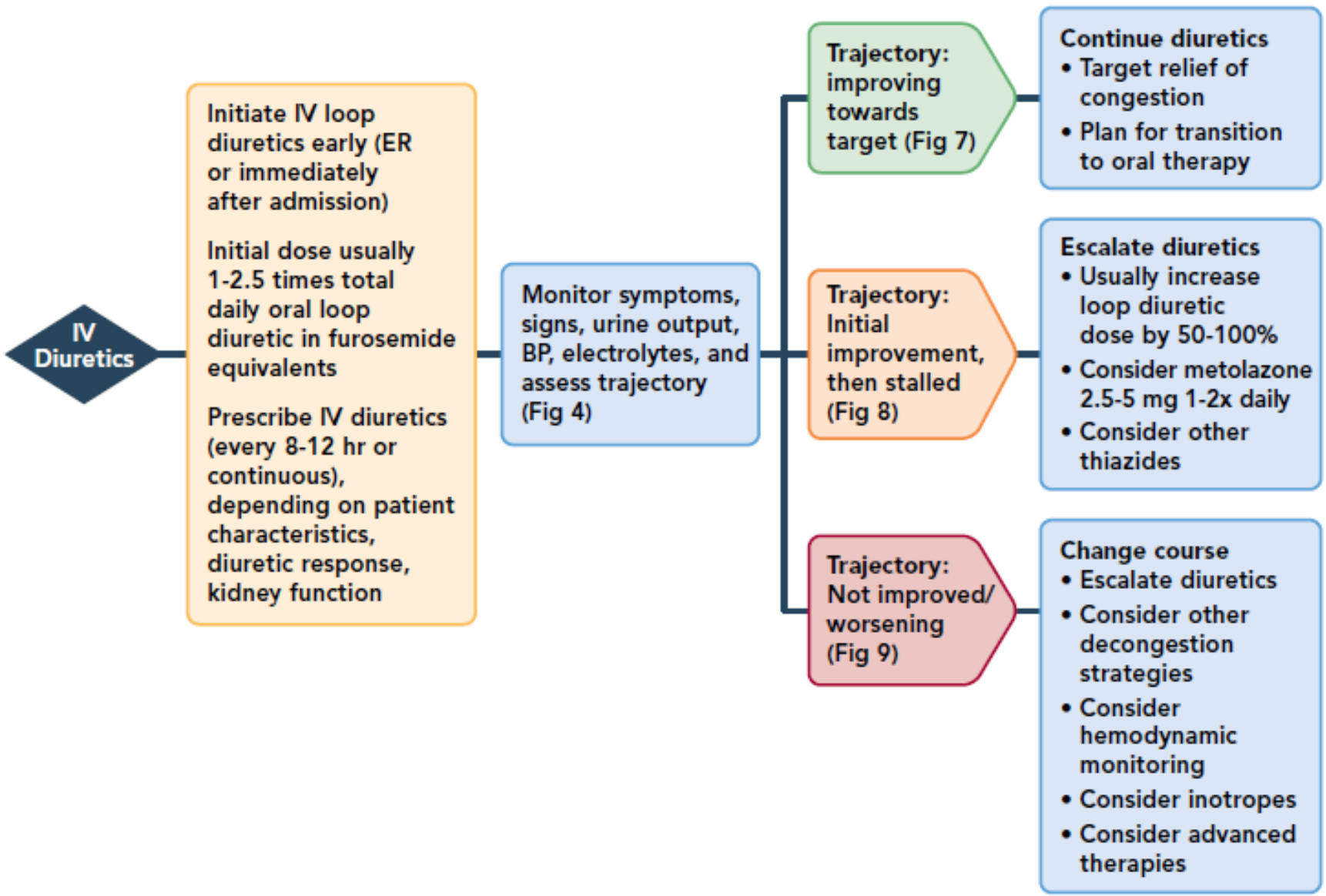
Prescribe IV diuretics (every 8-12 hr or continuous), depending on patient characteristics, diuretic response, kidney function

Monitor symptoms, signs, urine output, BP, electrolytes, and assess trajectory (Fig 4)

Hollenberg SM, JACC 2019; 74915):1966

Felker M, JACC 2021:709-12

Trajectory Check for Diuretic Response



Loop diuretics

- First line therapy

Thiazides and metolazone

- Effective distal tubule diuretics for diuretic resistance
- Can worsen hypoK, hypoNa and renal function

Mineralocorticoid receptor antagonists

acetazolamide

Hypertonic saline

- Limited evidence

ultrafiltration

Hollenberg SM, JACC 2019; 74915):1966

Cycle of Uncertainty and Ineffectiveness for In-Hospital Use of Diuretic Therapy

Uncertainty in the Assessment of Congestion

- Congestion variably graded by clinicians
- Multiple markers (e.g., exam, symptoms, weight), each with limitations and potential for conflicting information

Uncertainty in Optimal Diuretic Therapy and Strategy

- Best type, dose, and frequency of diuretic therapy is unclear
- Choice of diuretic and dose subject to clinician discretion with significant variability

High Rates of Mortality and Readmission

- ~90% of patients receive IV diuretic therapy
- Up to 20-30% of patients recorded as minimal to no weight loss (or weight gain) during hospitalization
- 2-4% in-hospital mortality in the United States
- Many patients discharged with significant residual congestion (e.g., high natriuretic peptides, clinical exam)
- No widely adopted, standardized, or evidence-based discharge criteria
- ~1 in 4 patients die or are readmitted within 30 days of discharge

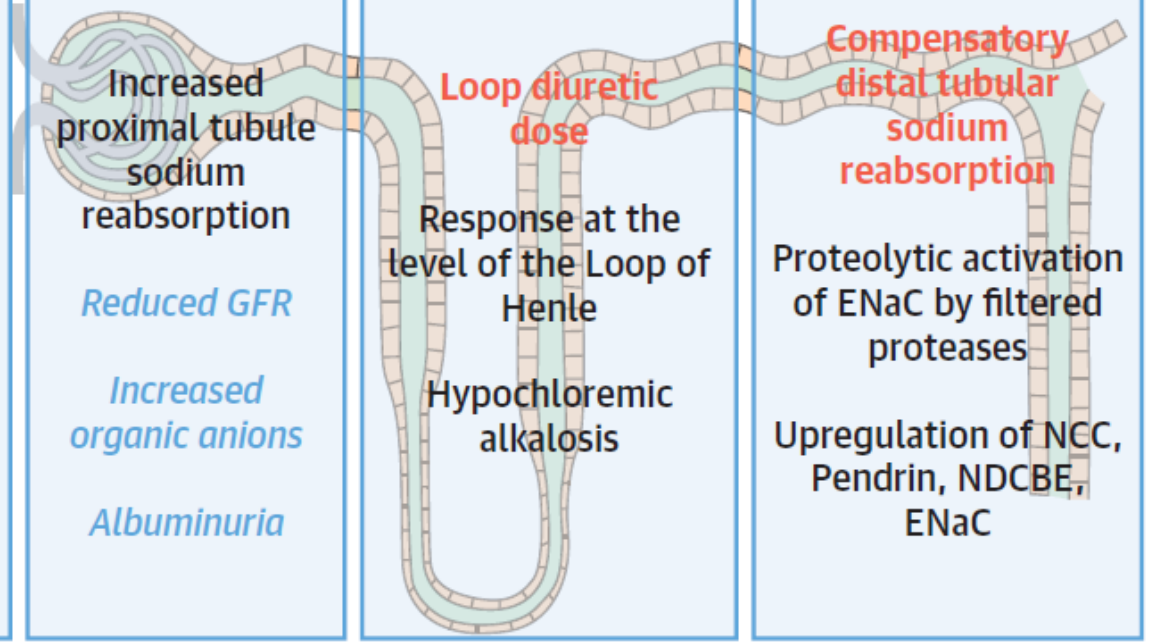
Uncertainty in Grading Response to Diuretic Therapy

- Multiple markers for assessing diuretic response, each with limitations and potential for conflicting information
- Variable reliability of congestion data in real-world practice (e.g., daily weights, net fluid loss, urine output)

Felker M, JACC 2021:709-12

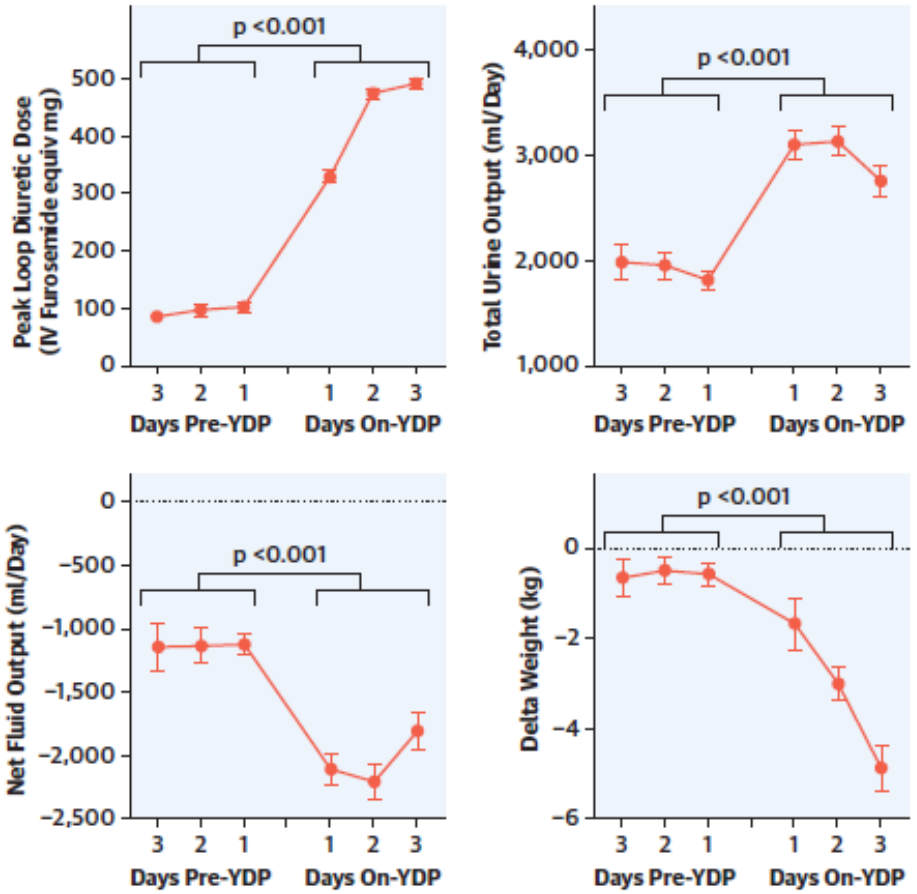
Understanding Mechanisms of Diuretic Resistance

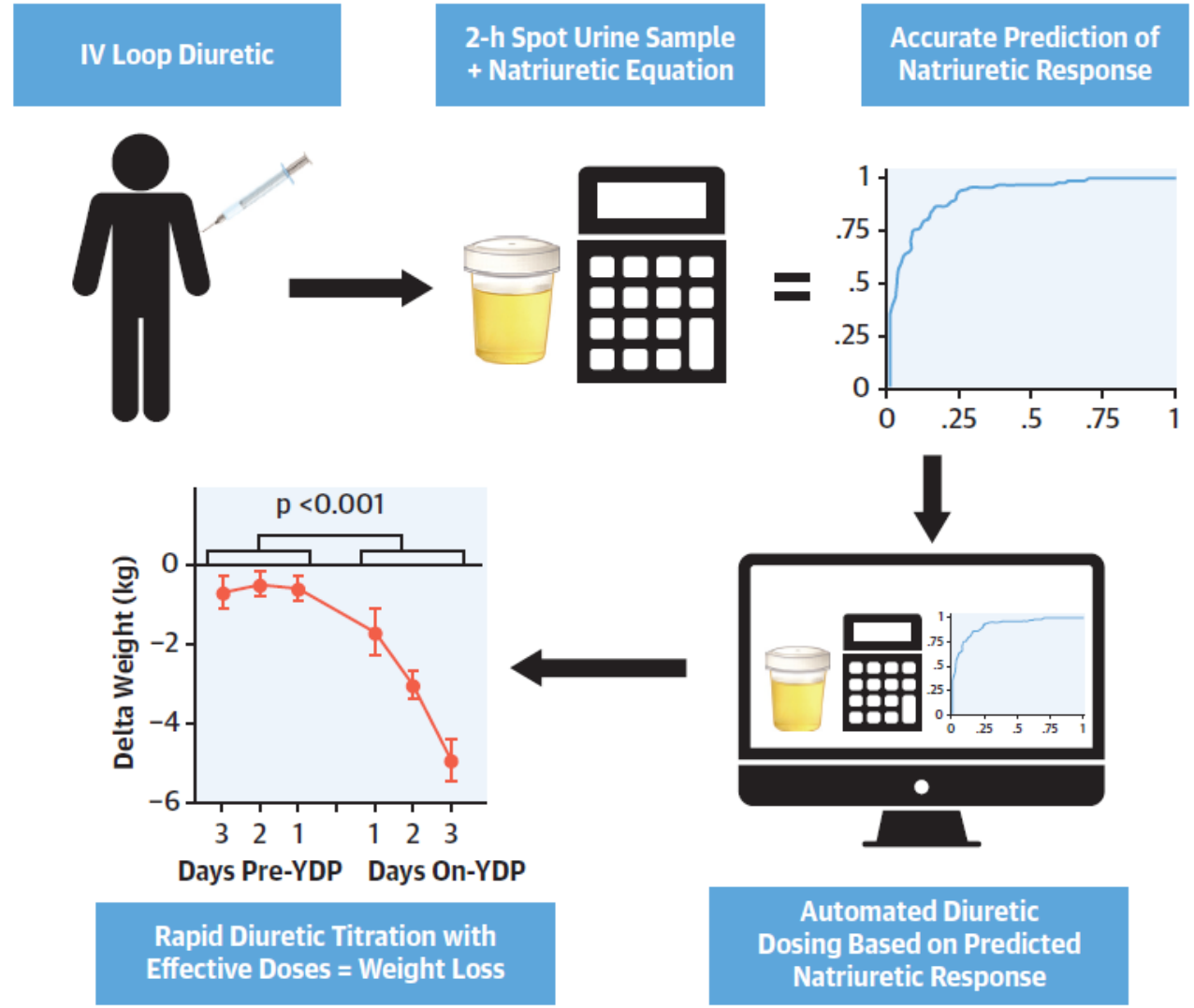
Importance of specific cause/mechanism on diuretic resistance	Diuretic Resistance Categorization			
	Pre-Renal	Intra-Renal		
		Pre-Loop of Henle	Loop of Henle	Post-Loop of Henle
Significant	Venous congestion	Increased proximal tubule sodium reabsorption	Loop diuretic dose	Compensatory distal tubular sodium reabsorption
Unknown but hypothesized to be significant	Increased intra-abdominal pressure	*Reduced GFR*	Response at the level of the Loop of Henle	Proteolytic activation of ENaC by filtered proteases
Not significant with the mild to moderate derangement found in the average HF patient	*Reduced cardiac output*	*Increased organic anions*	Hypochloremic alkalosis	Upregulation of NCC, Pendrin, NDCBE, ENaC
	Hypoalbuminemia	*Albuminuria*		
	High sodium intake			



Felker, JACC 2020:1178-95

Is There a Better Way? Monitoring Urine Sodium Strategy

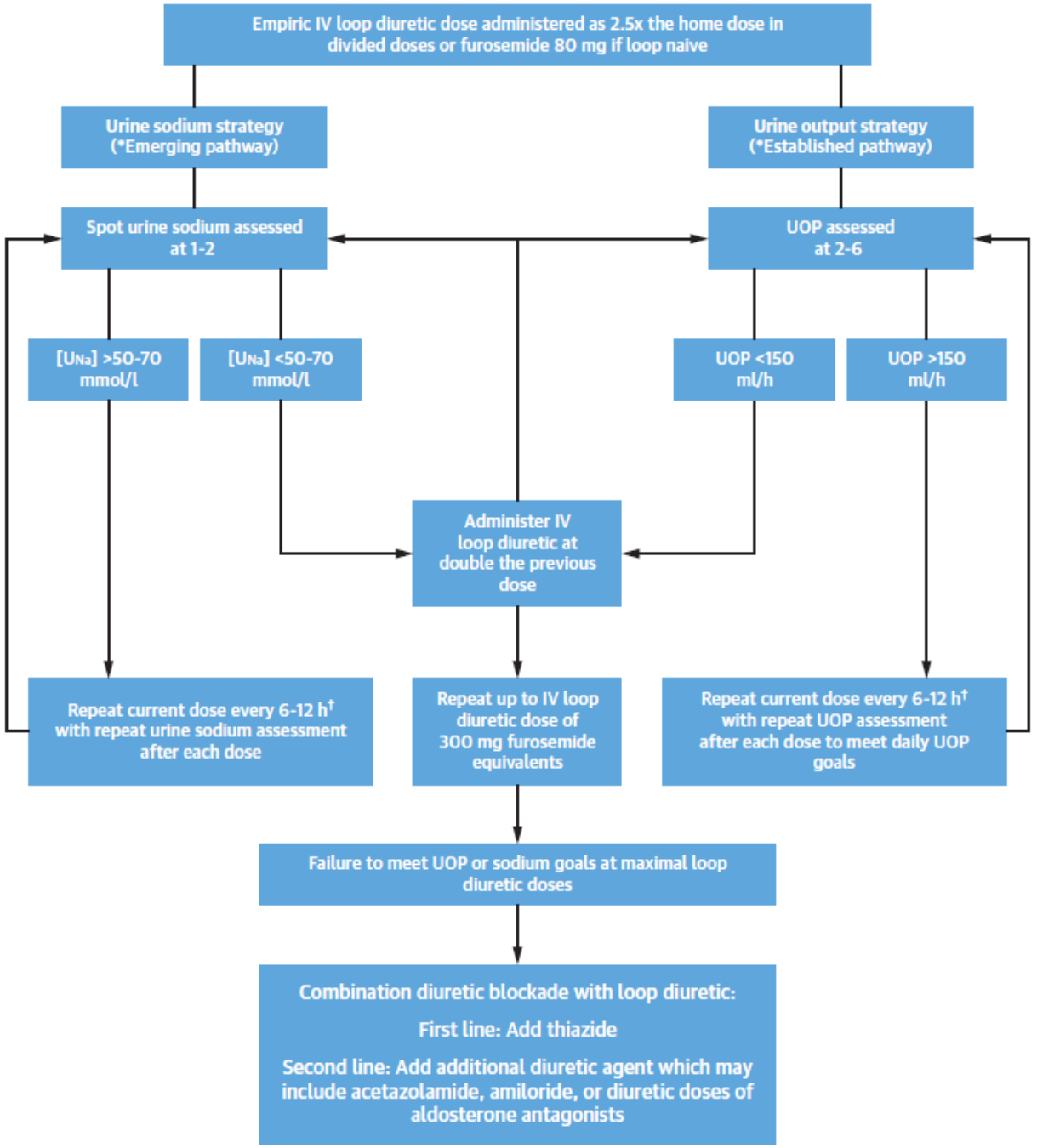




Rao, V.S. et al. J Am Coll Cardiol. 2021;77(6):695-708.

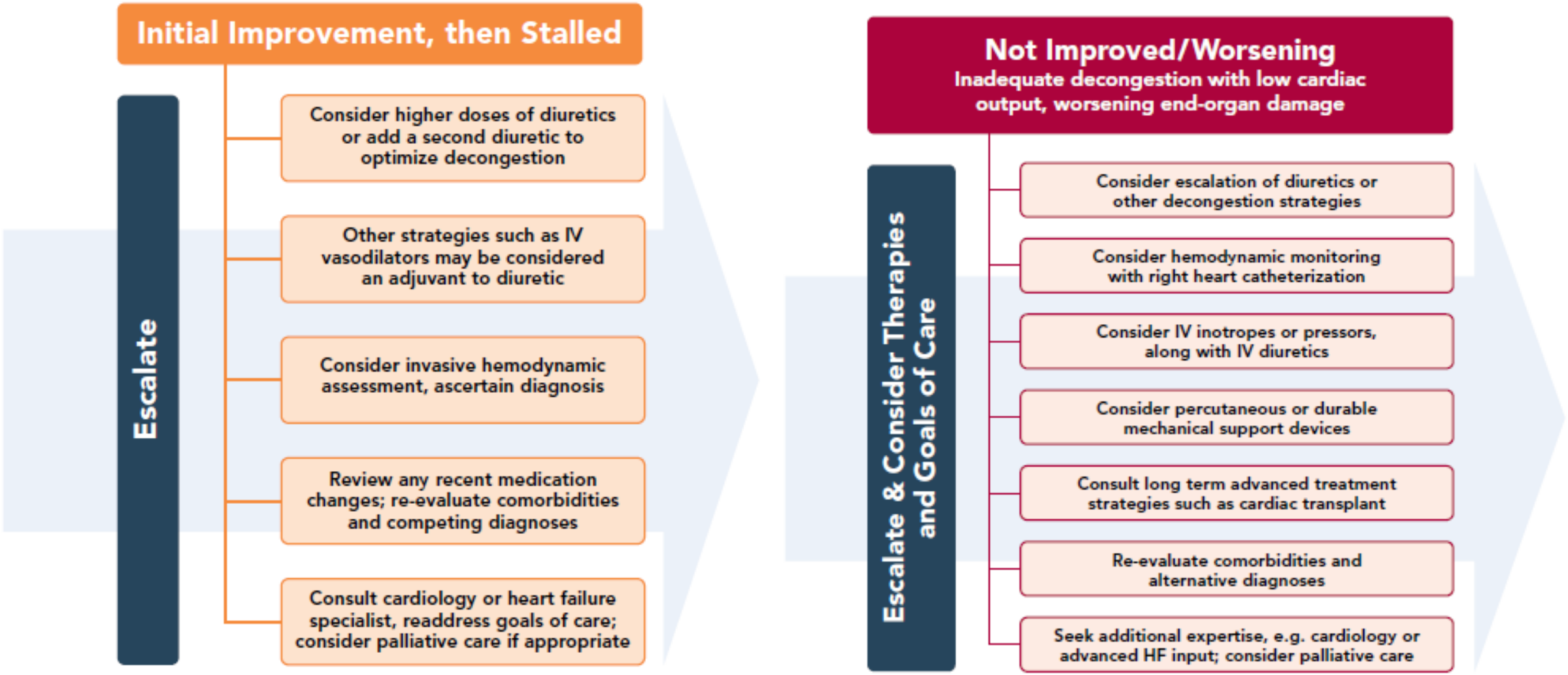
Rao et al: JACC 2021:695-708

Proposal for Diuretic Titration



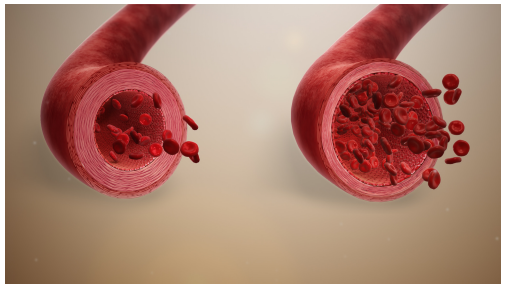
Felker, JACC 2020:1178-95

What Can I Do When it is Not Working??



Hollenberg SM, JACC 2019; 74915):1966

Vasodilators in Acute Heart Failure Syndromes



Who?

- SBP>100 mmHg
- Acute Pulmonary Edema
- AHF with acute ischemia

What?

- IV nitroglycerin
- IV nitroprusside

When?

- Early on in stabilization phase
- Failure to respond to diuretics
- No need for direct inotropic support

Why?

- Arterial vasodilation to reduce afterload, LV and RV filling pressures
- Increased venous capacitance to reduce preload
- Redistribute blood away from pulmonary circulation

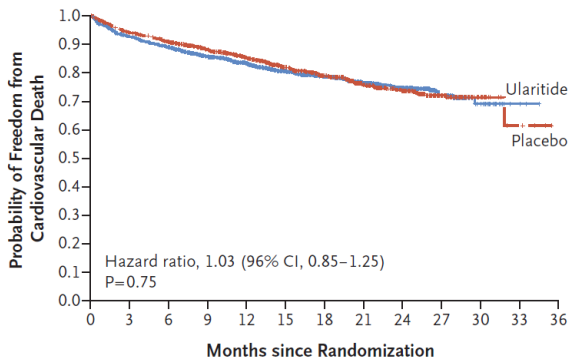
Vasodilators in Acute Heart Failure Syndromes

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

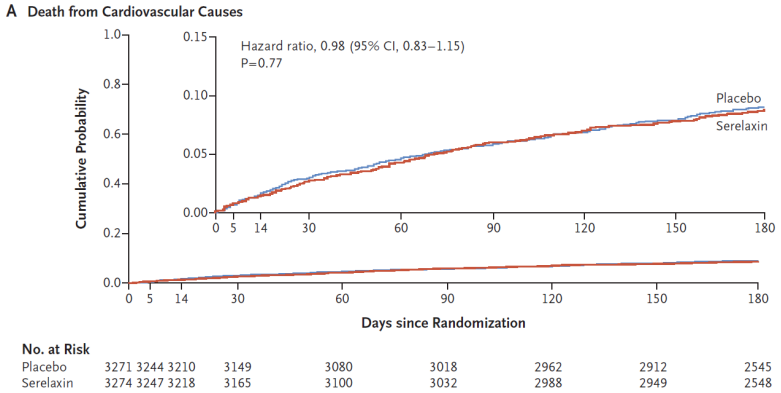
Effect of Ularitide on Cardiovascular Mortality in Acute Heart Failure

M. Packer, C. O'Connor, J.J.V. McMurray, J. Wittes, W.T. Abraham, S.D. Anker, K. Dickstein, G. Filippatos, R. Holcomb, H. Krum,* A.P. Maggioni, A. Mebazaa, W.F. Peacock, M.C. Petrie, P. Ponikowski, F. Ruschitzka, D.J. van Veldhuisen, L.S. Kowarski, M. Schactman, and J. Holzmeister, for the TRUE-AHF Investigators†



No. at Risk

Ularitide	1088	988	942	789	669	546	456	356	234	106	26	2	0
Placebo	1069	987	934	786	668	547	444	338	219	104	19	5	0



No. at Risk

Placebo	3271 3244 3210	3149	3080	3018	2962	2912	2545
Serelaxin	3274 3247 3218	3165	3100	3032	2988	2949	2548

ORIGINAL ARTICLE

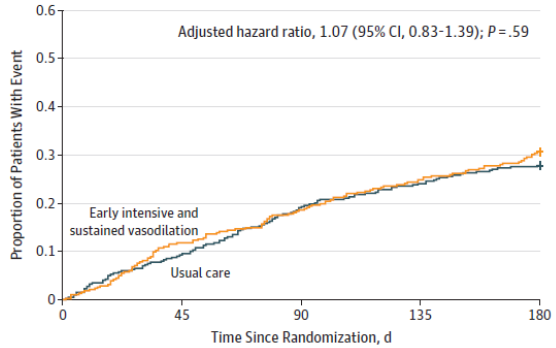
Effects of Serelaxin in Patients with Acute Heart Failure

M. Metra, J.R. Teerlink, G. Cotter, B.A. Davison, G.M. Felker, G. Filippatos, B.H. Greenberg, P.S. Pang, P. Ponikowski, A.A. Voors, K.F. Adams, S.D. Anker, A. Arias-Mendoza, P. Avendaño, F. Bacal, M. Böhm, G. Bortman, J.G.F. Cleland, A. Cohen-Solal, M.G. Crespo-Leiro, M. Dorobantu, L.E. Echeverría, R. Ferrari, S. Goland, E. Goncalvesová, A. Goudev, L. Køber, J. Lema-Osores, P.D. Levy, K. McDonald, P. Manga, B. Merkely, C. Mueller, B. Pieske, J. Silva-Cardoso, J. Špinar, I. Squire, J. Stępińska, W. Van Mieghem, D. von Lewinski, G. Wikström, M.B. Yilmaz, N. Hagner, T. Holbro, T.A. Hua,* S.V. Sabarwal, T. Severin, P. Szecsödy, and C. Gimpelewicz, for the RELAX-AHF-2 Committees Investigators†

JAMA | Original Investigation

Effect of a Strategy of Comprehensive Vasodilation vs Usual Care on Mortality and Heart Failure Rehospitalization Among Patients With Acute Heart Failure
The GALACTIC Randomized Clinical Trial

Figure 2. Kaplan-Meier Estimates of the Primary End Point of Cumulative All-Cause Mortality or Acute Heart Failure Rehospitalization Within 180 Days Among Patients Treated With Early Intensive and Sustained Vasodilation vs Usual Care



No. at risk

Early intensive and sustained vasodilation	382	337	311	287	265
Usual care	399	361	322	303	288

NEJM 2017; 376:1956-64 *NEJM 2019; 381:716-26* *JAMA 2019; 322:2292-2302*

Inotropic Use in Acute Heart Failure Syndromes

Who?

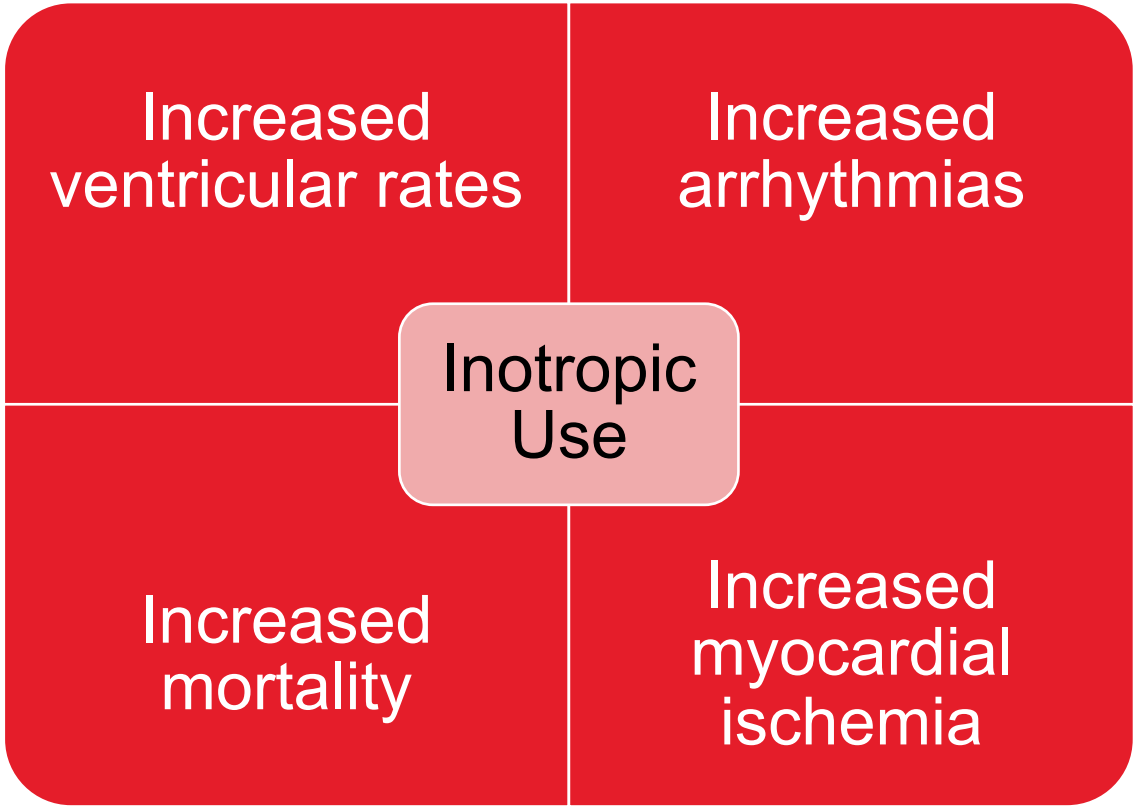
- Evidence of hypoperfusion and hypotension
- Cardiogenic shock

What?

- IV milrinone
- IV dobutamine

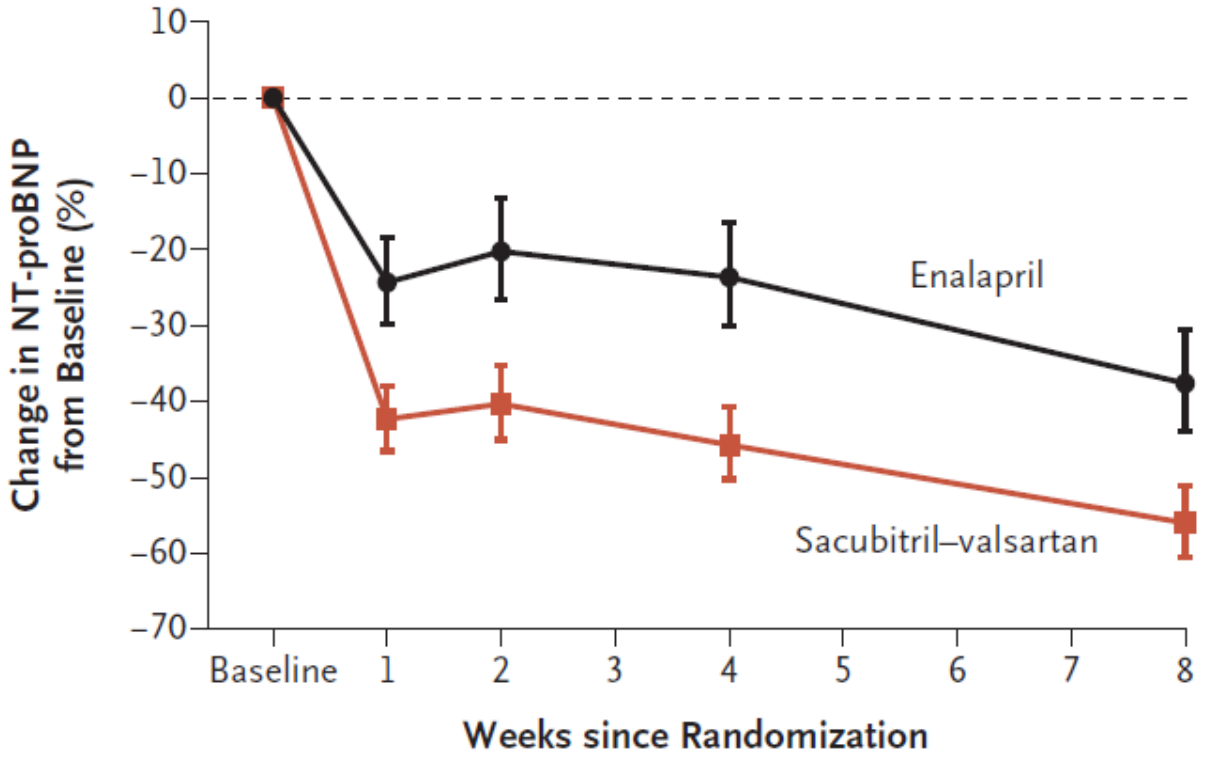
When?

- Typically, short term use
- Lowest effective dose for shortest duration
- Adequate monitoring and risk prevention essential



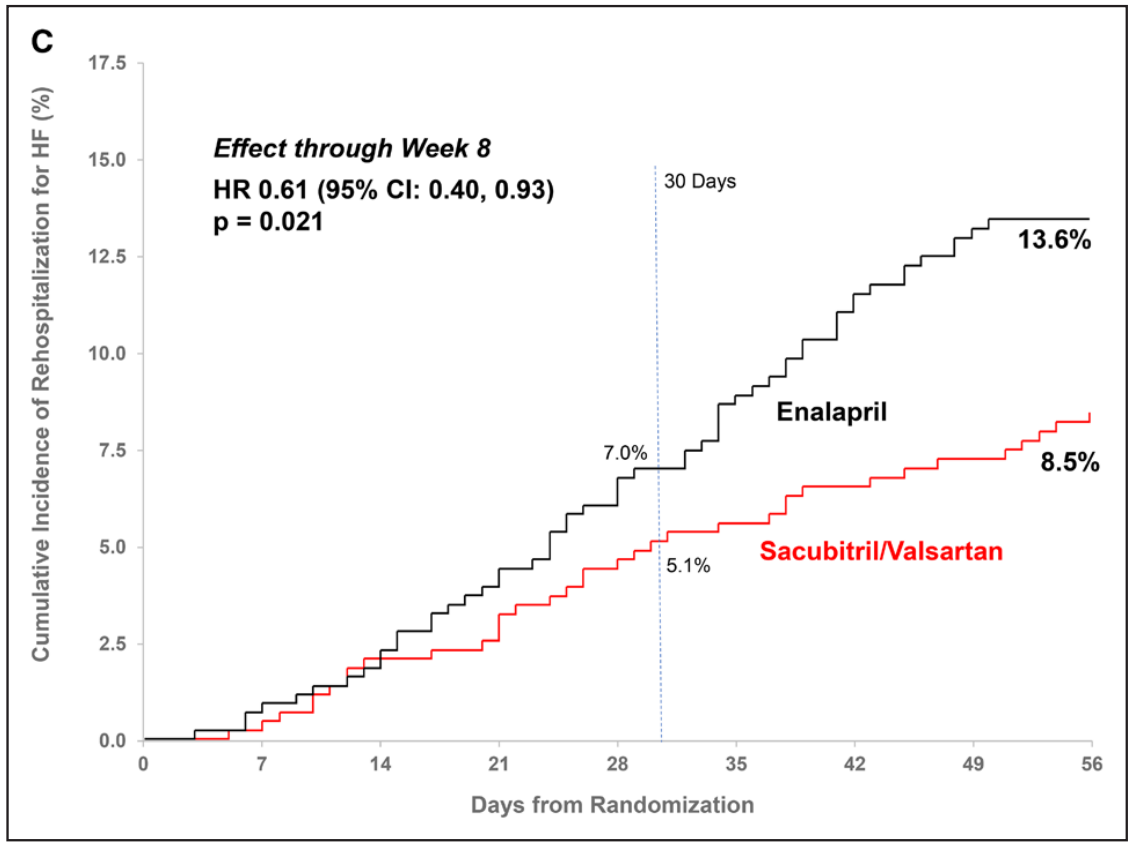
Transition to Oral Therapies

Pioneer-HF Study: ARNI in Acute Decompensated HF



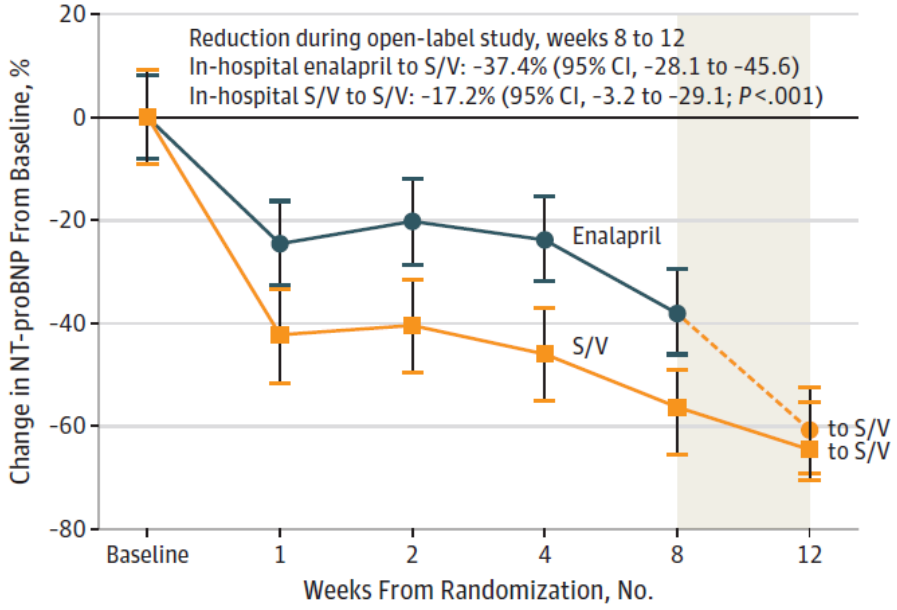
No. at Risk

Enalapril	394	359	351	350	348
Sacubitril–valsartan	397	355	363	365	349



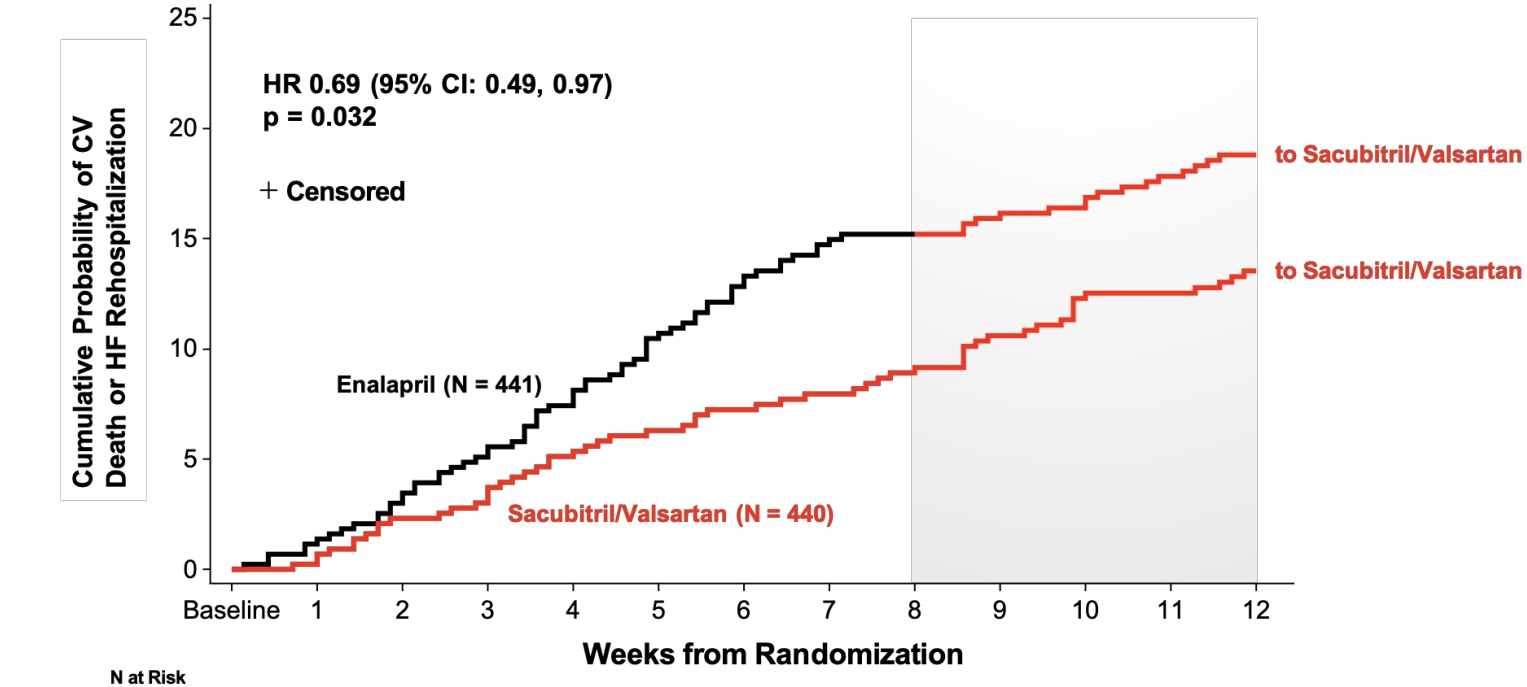
New Eng J Med 2019;380:539-48

Pioneer-HF Study: Secondary Analysis of Open Label Extension



No. at risk

Enalapril	394	359	351	350	348	335
S/V	397	355	363	365	349	340



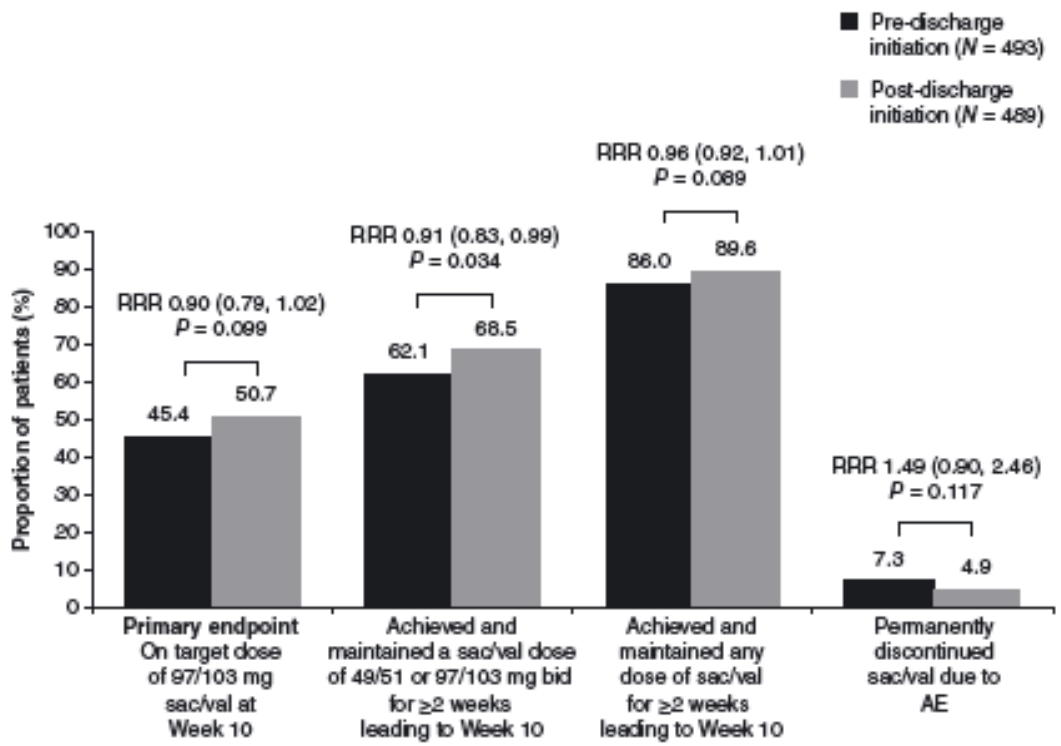
N at Risk

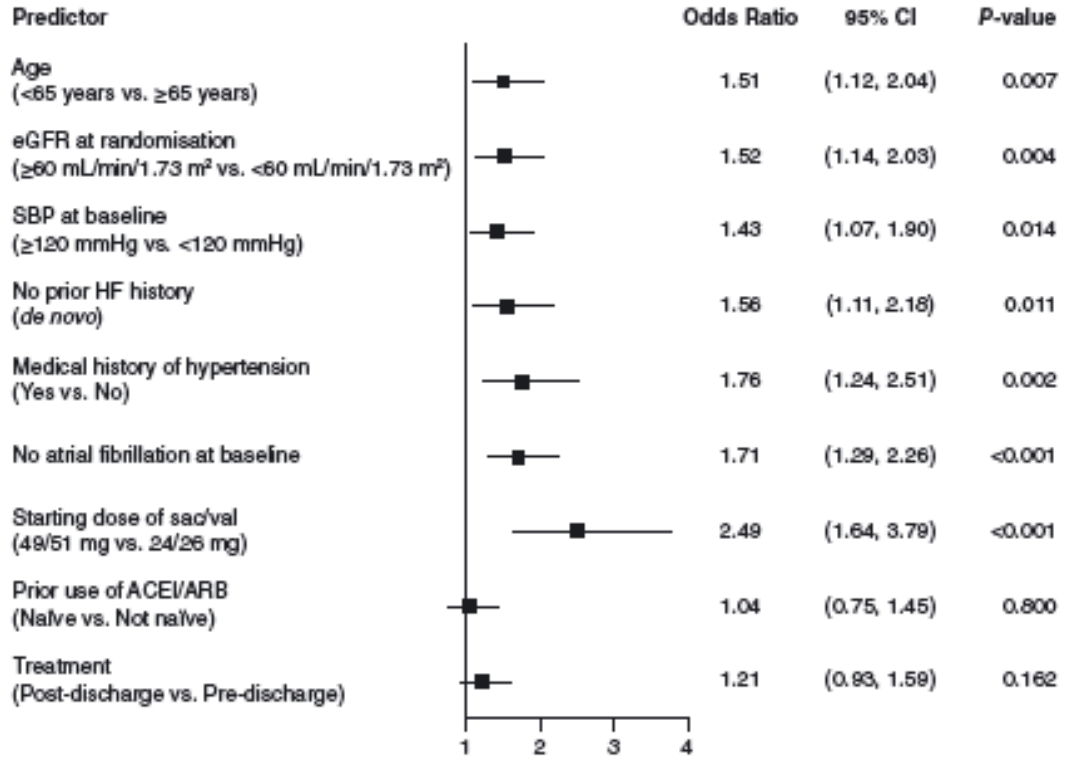
Enalapril (n)	441	429	418	407	396	381	368	359	356	353	351	342	296
Sacubitril/Valsartan (n)	440	434	420	415	404	397	390	385	380	371	362	358	295

These data include adjudicated HF hospitalizations

JAMA Cardiol 2020; 5: 202-207

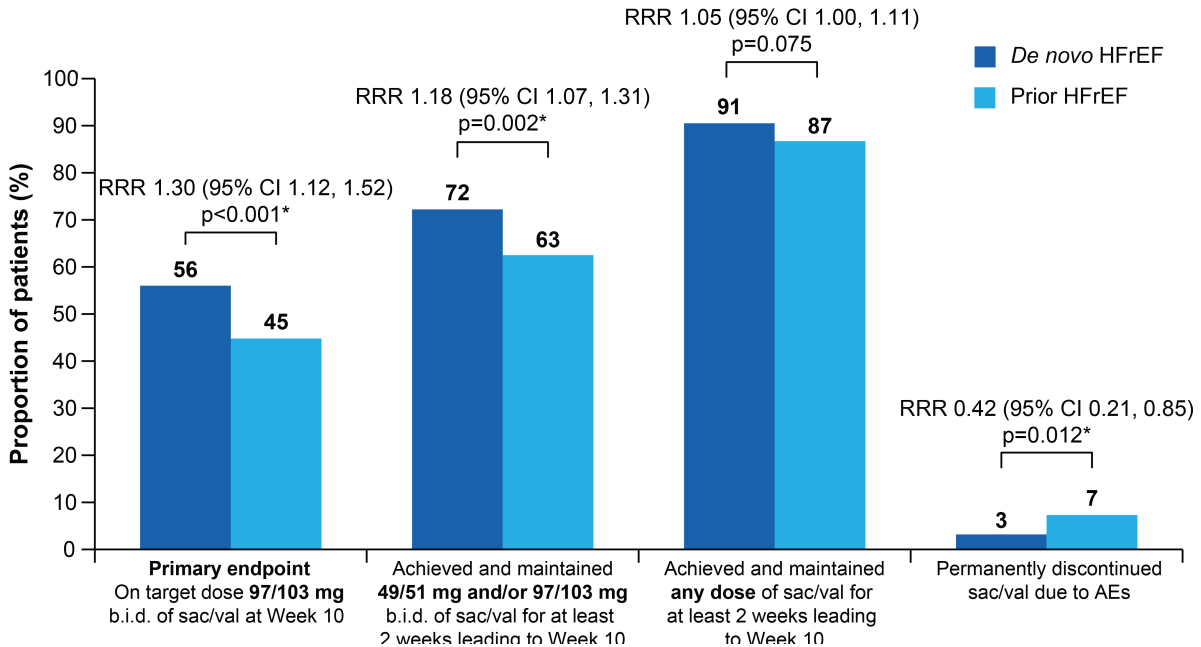
TRANSITION Study: Initiation of Sacubitril/valsartan in ADHF in Hospital or Shortly After Discharge

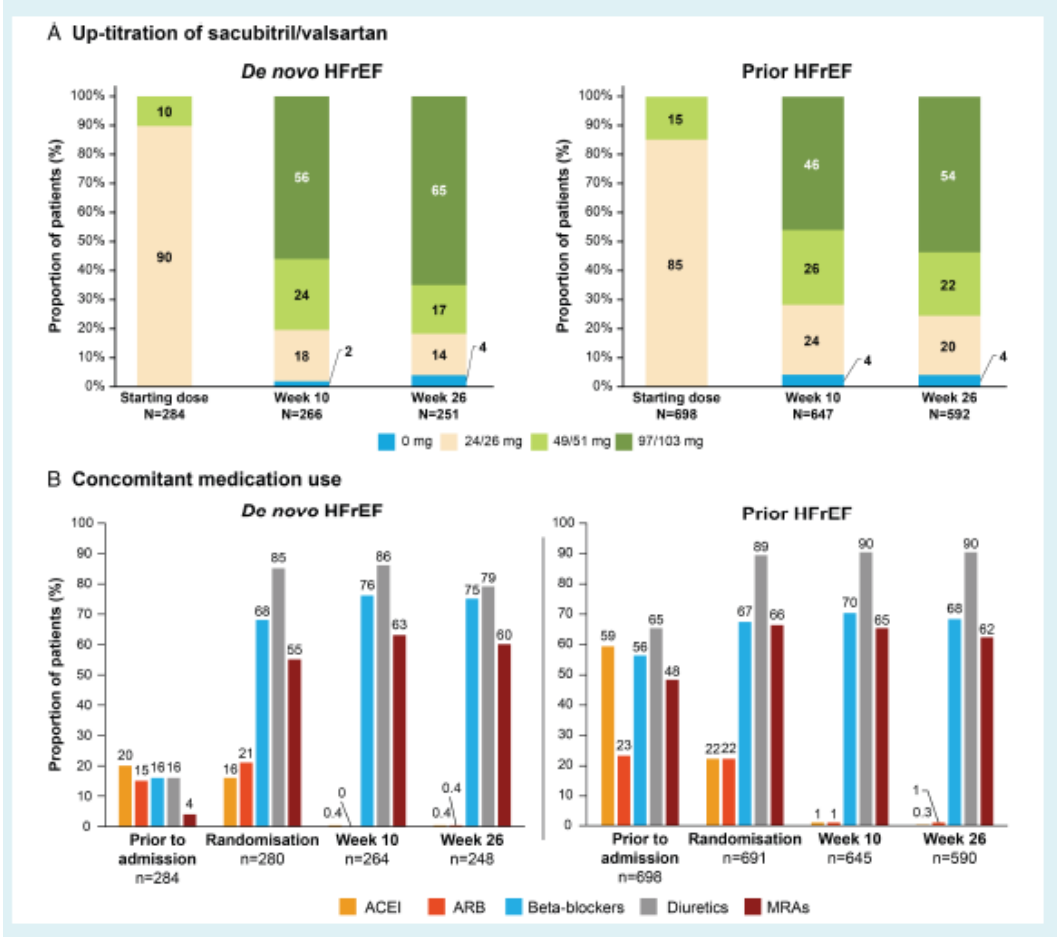




Wachter et al. Eur J HF; 2019: 21:998-1007

Transition Sub-Study: What About Newly Diagnosed Patients?

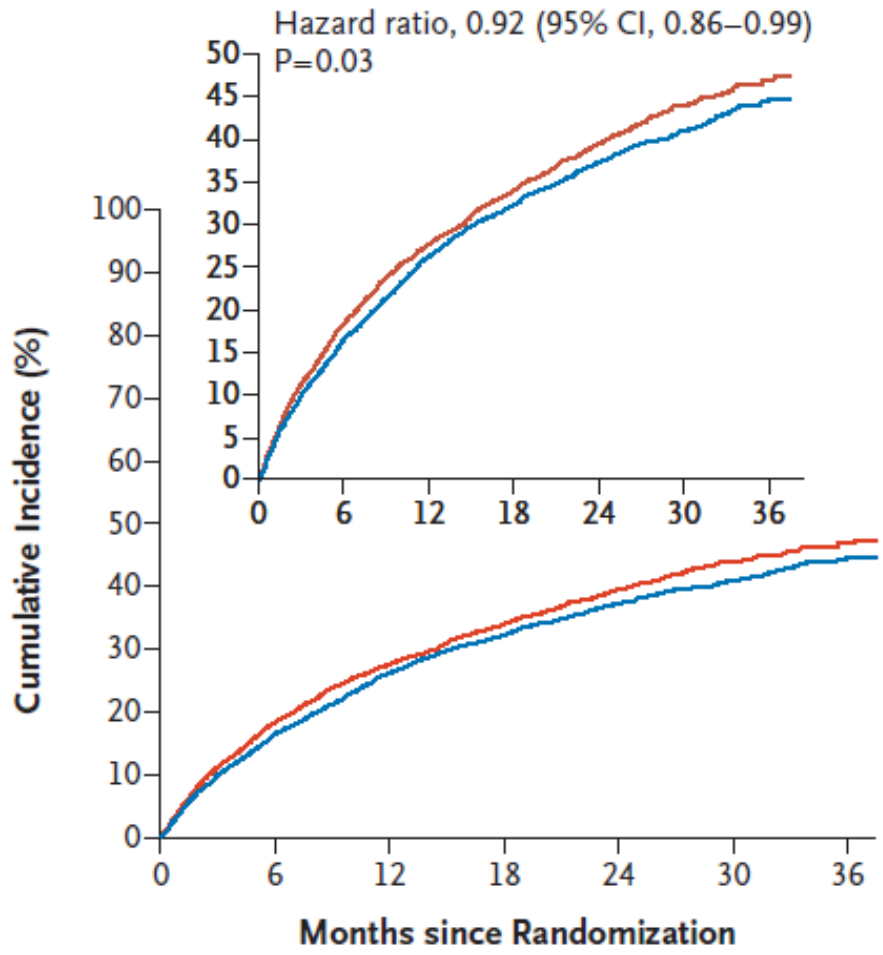




Senni et al; Eur J HF 2020; 22:303-312

GALACTIC-HF: Omecamtiv Mecarbil in High-Risk Heart Failure

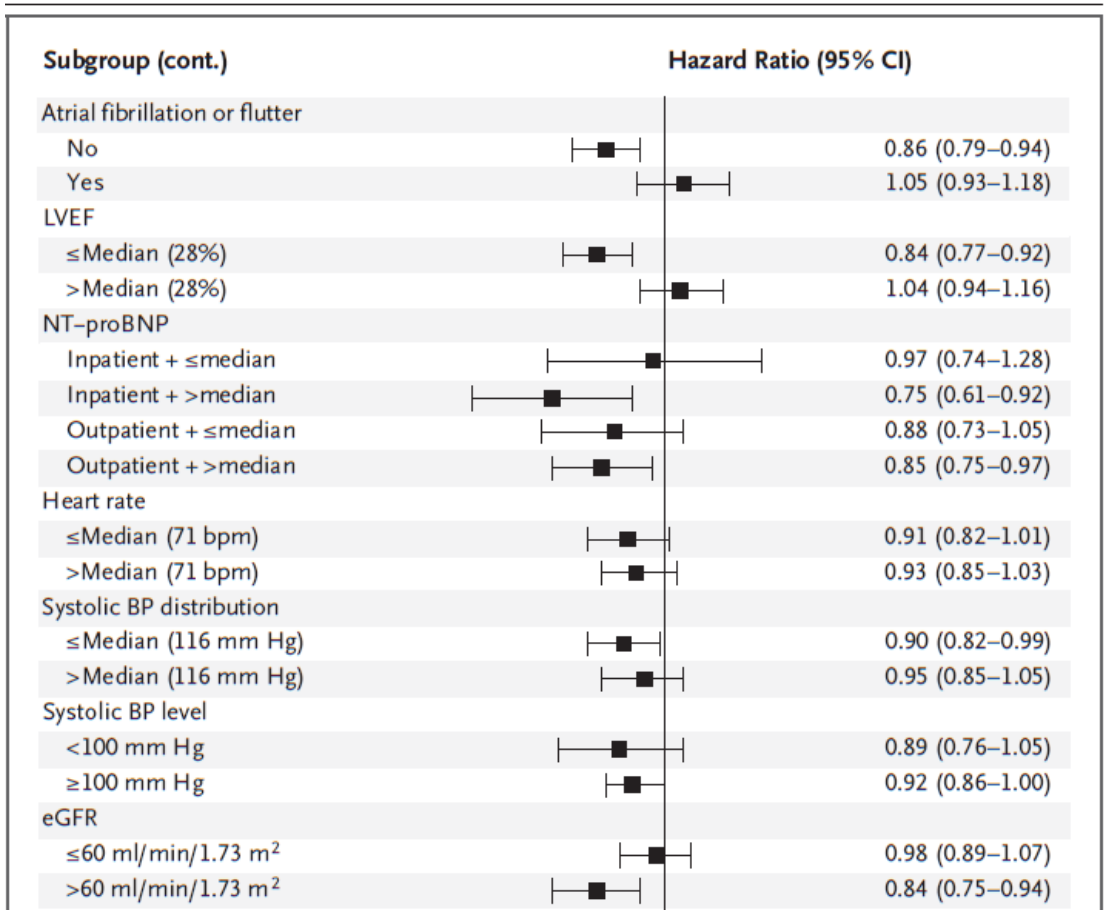
A Primary Outcome



No. at Risk

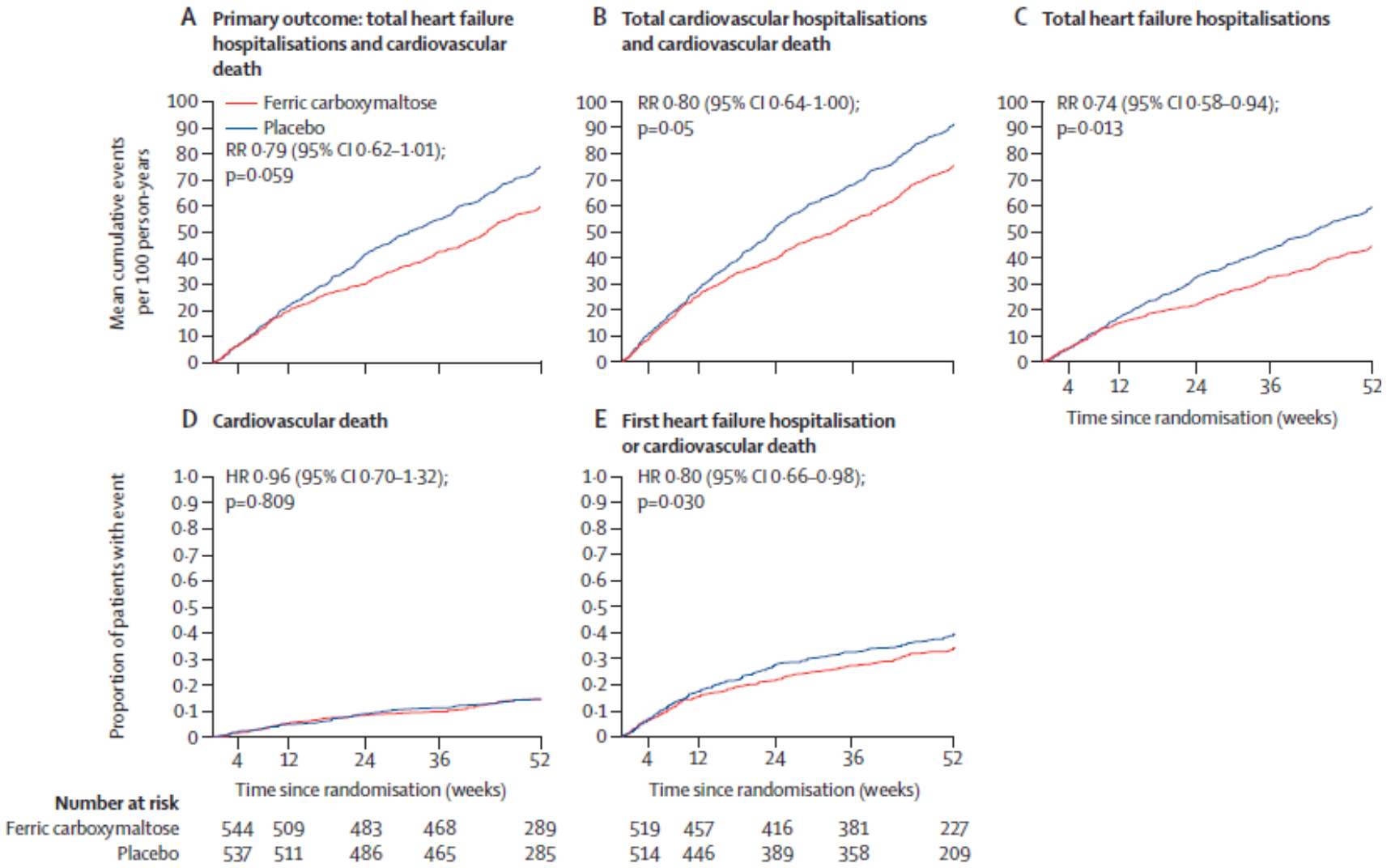
Placebo	4112	3310	2889	2102	1349	647	141
Omecamtiv mecarbil	4120	3391	2953	2158	1430	700	164

Primary endpoint HR for Acute HF: 0.89 (95%CI 0.78-1.01)



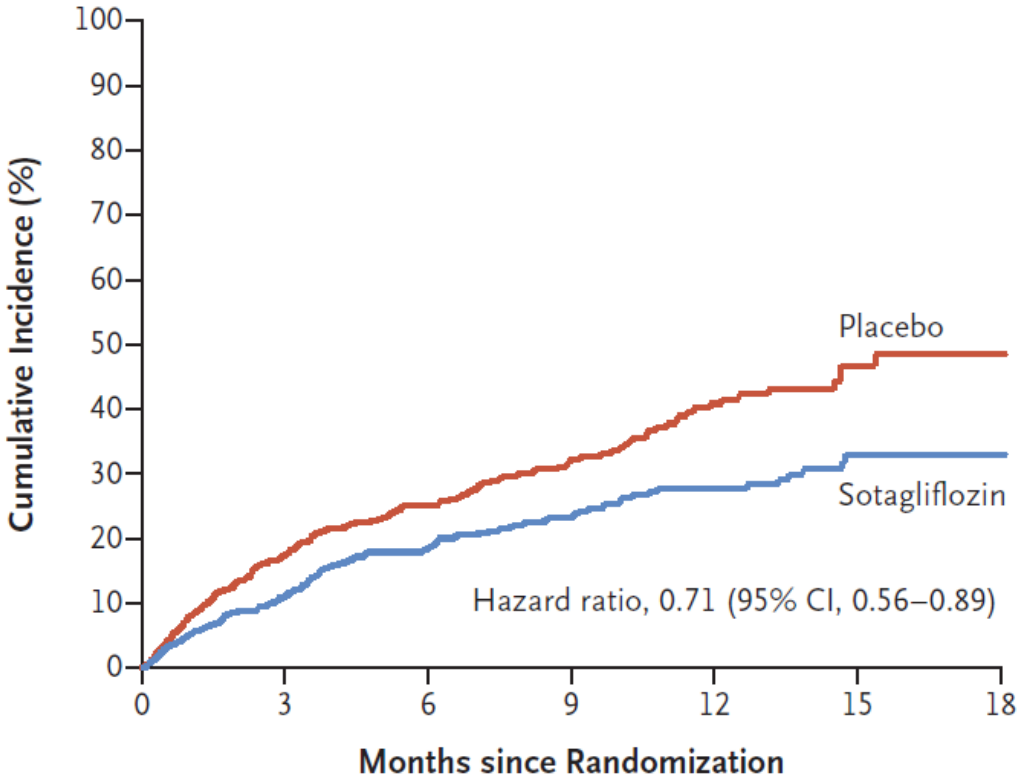
NEJM 2021; 384:105-16

AFFIRM-HF: Ferric Carboxymaltose in Iron Deficient Acute HF Patients



Poikowski, Lancet 2020; 396:1895

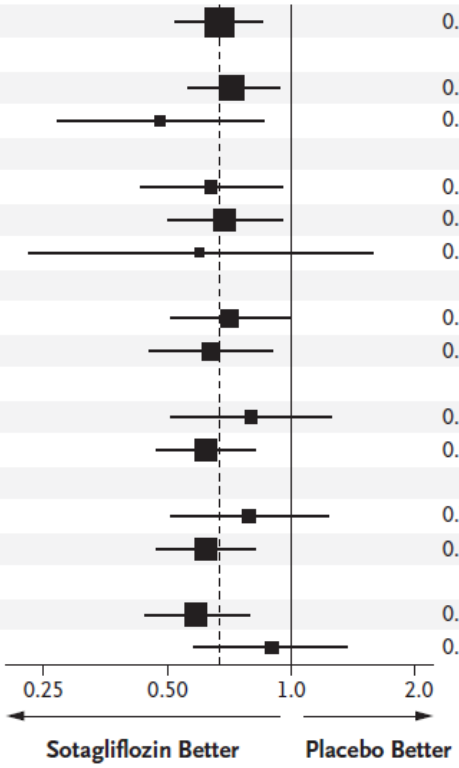
Sotagliflozin in Patients with DM and Recent Hospitalization for Acute HF



No. at Risk

Placebo	614	461	345	241	144	66	14
Sotagliflozin	608	498	374	266	171	76	25

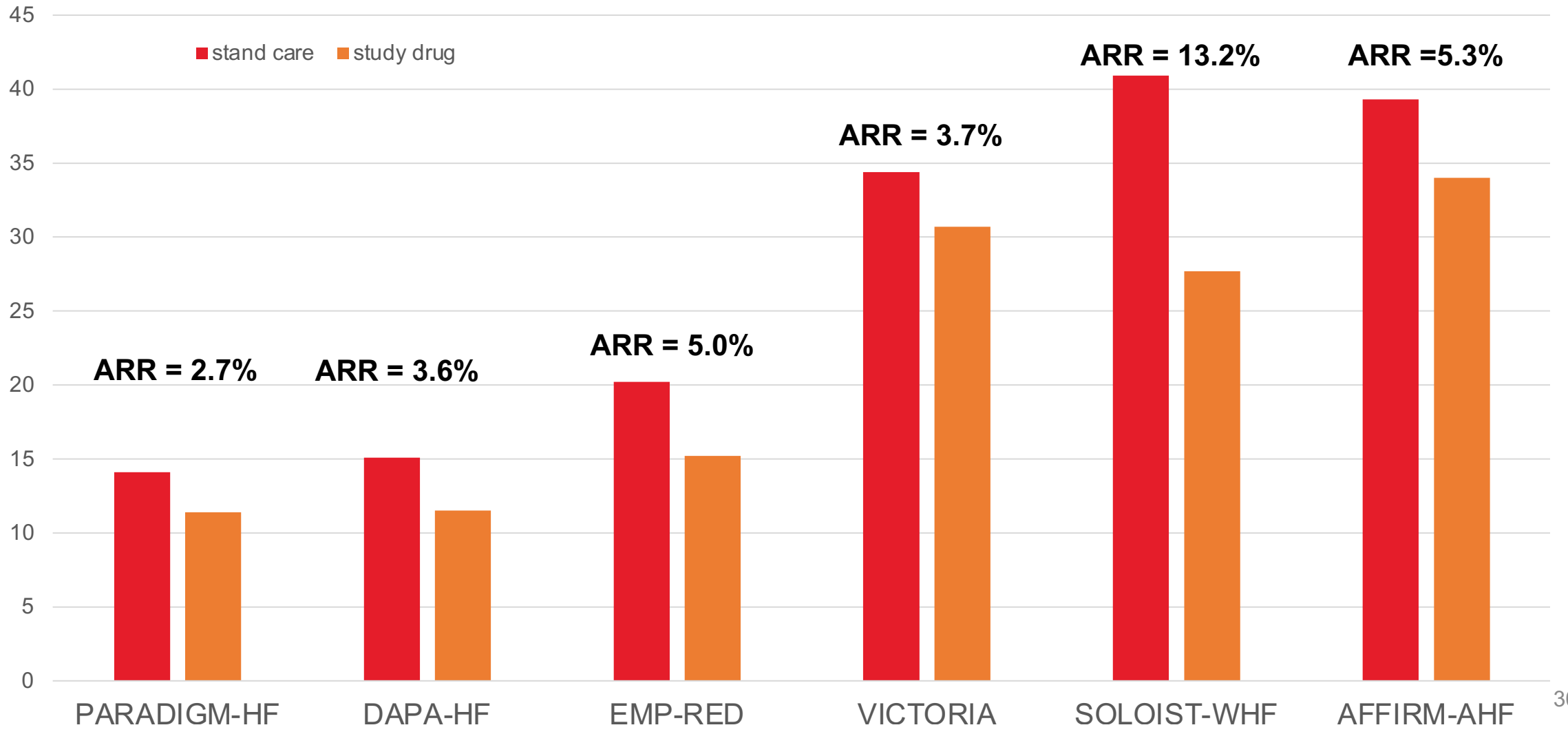
Subgroup	No. of Patients	Sotagliflozin	Placebo	Hazard Ratio (95% CI)
		events per 100 patient-yr		
Overall	1222	51.0	76.3	0.67 (0.52–0.85)
LVEF				
<50%	966	56.9	79.9	0.72 (0.56–0.94)
≥50%	256	30.6	64.0	0.48 (0.27–0.86)
Geographic region				
North America or Latin America	346	68.3	103.0	0.64 (0.43–0.95)
Europe	800	44.1	64.7	0.69 (0.50–0.95)
Rest of the world	76	48.4	78.3	0.60 (0.23–1.58)
Timing of first dose				
Before discharge	596	52.1	76.6	0.71 (0.51–0.99)
After discharge	626	50.0	76.1	0.64 (0.45–0.90)
Sex				
Female	412	41.9	52.0	0.80 (0.51–1.25)
Male	810	55.7	89.3	0.62 (0.47–0.82)
Age				
<65 yr	364	57.1	71.1	0.79 (0.51–1.23)
≥65 yr	858	48.0	78.5	0.62 (0.47–0.82)
Estimated GFR				
<60 ml/min/1.73 m^2	854	50.1	85.8	0.59 (0.44–0.79)
≥60 ml/min/1.73 m^2	368	53.1	58.1	0.90 (0.58–1.37)



Bhatt . NEJM 2021; 384:117-28

Treatment Effects in Recent RCT Enrolling Patients with Acute HF

First Occurrence of Either CV death or Heart Failure Hospitalization at 12 months



Summary of Treatment Algorithm in Acute Heart Failure