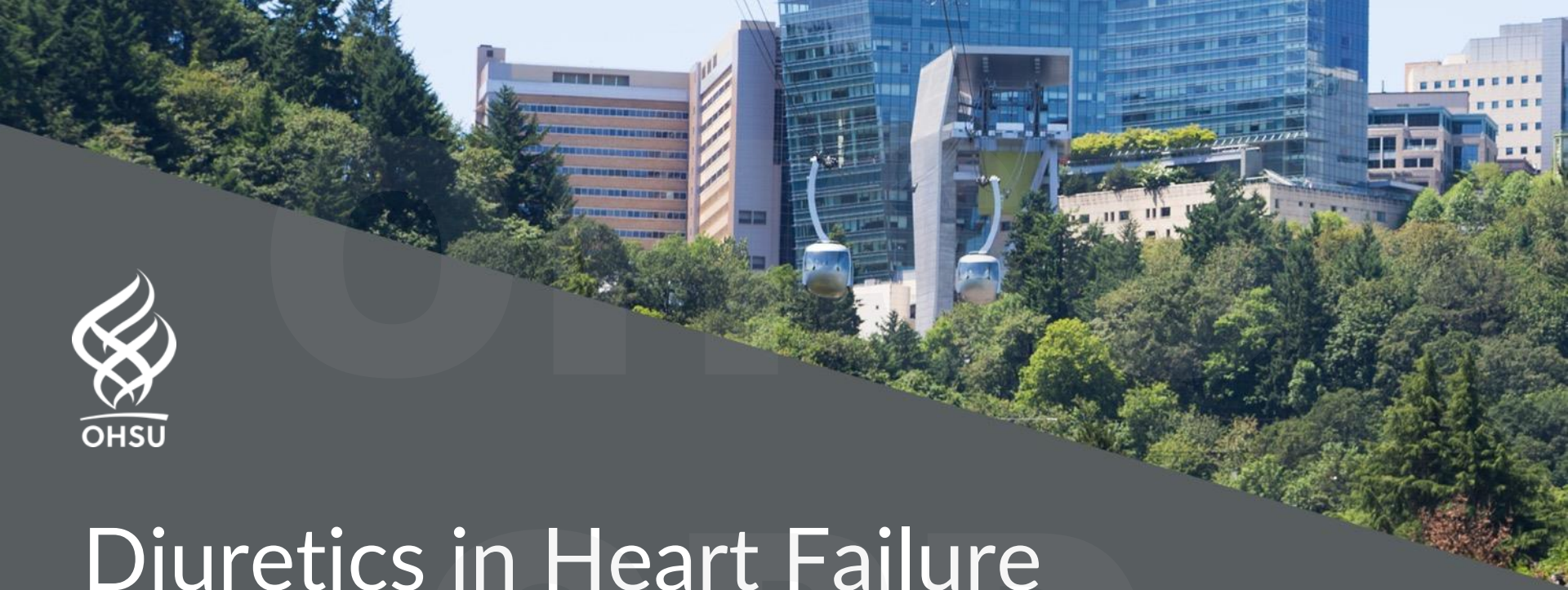

Diuretics in Heart Failure

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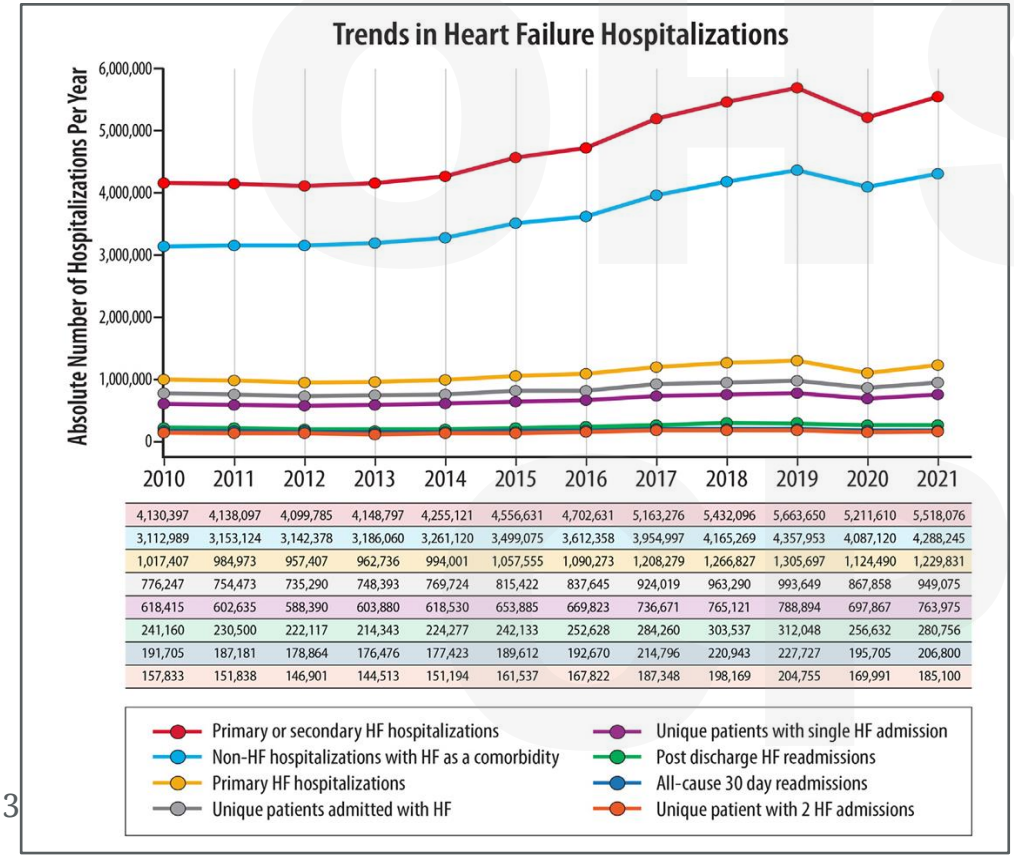
9.11.2025

Disclosures

- None relevant to this talk
- Consulting/Clinical Trials: Boston Scientific, Biotronik, Viscardia

Heart failure hospitalizations



Bozkurt, et al. HF STATS, JCF 2024

Patient presentation

- 68-year-old man with heart failure due to ischemic CM
- Presents to the ER with weight gain, orthopnea, and dyspnea with ADLs
- Home HF medications: Entresto 24/26 mg BID, metoprolol 50 mg daily, spironolactone 25 mg daily, furosemide 40 mg PO BID
- Work up
  - Chest X-Ray – pulmonary edema
  - NT-proBNP 5400
  - Creatinine 1.6 (baseline 1.2)

What is the best diuretic choice?

(A) Furosemide 40 mg IV BID

(B) Bumetanide 2 mg IV BID

(C) Furosemide infusion 10 mg/hr

(D) Furosemide 40 mg IV BID + acetazolamide

(E) Furosemide 80 mg IV BID + metolazone

No right answer (maybe some wrong answers)

Evidenced based diuresis?

The NEW ENGLAND JOURNAL of MEDICINE

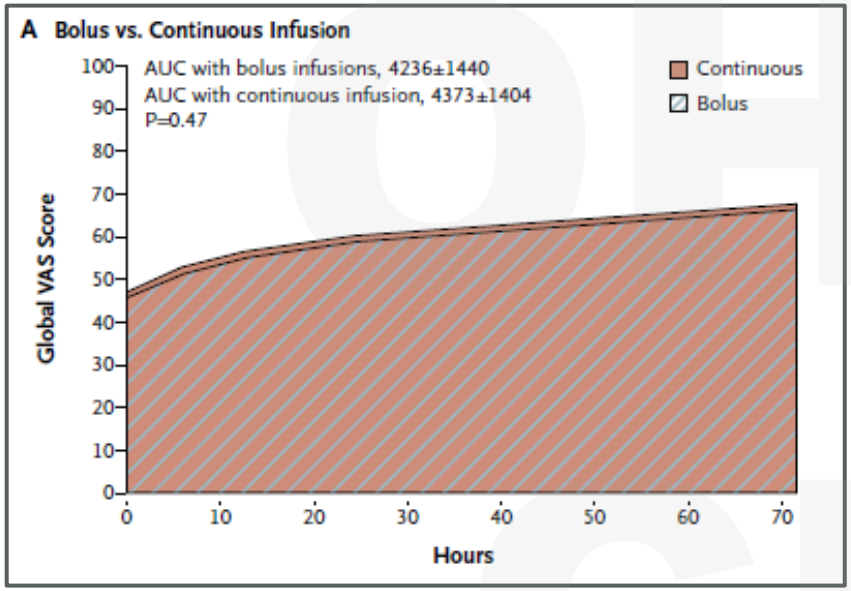
ESTABLISHED IN 1812 MARCH 3, 2011 VOL. 364 NO. 9

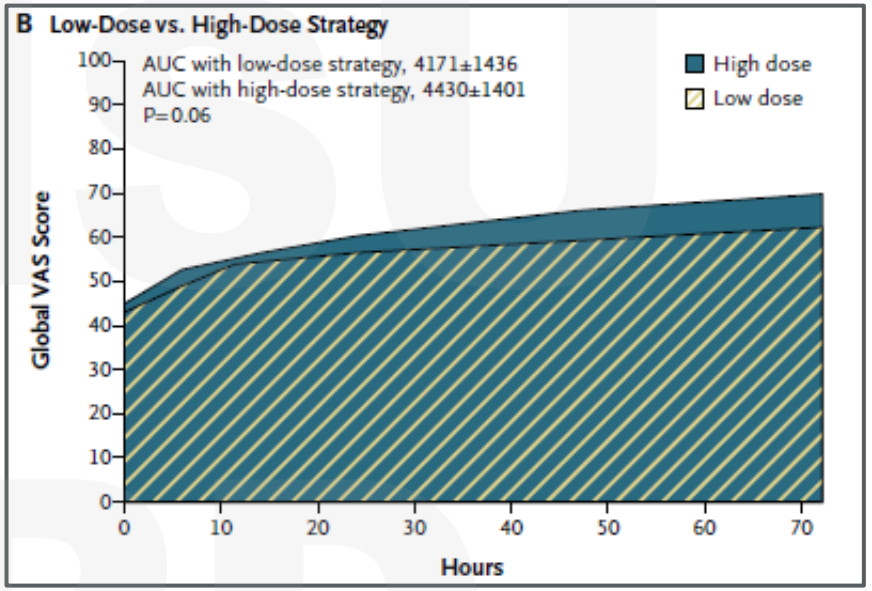
Diuretic Strategies in Patients with Acute Decompensated Heart Failure

G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., Anita Deswal, M.D., M.P.H.,

- Randomized controlled trial of 308 patients comparing
  - High dose (2.5x home dose IV) vs. low dose diuretic 1.0x home dose → IV)
  - Bolus vs. infusion
- Primary outcome: Symptoms

Nothing mattered





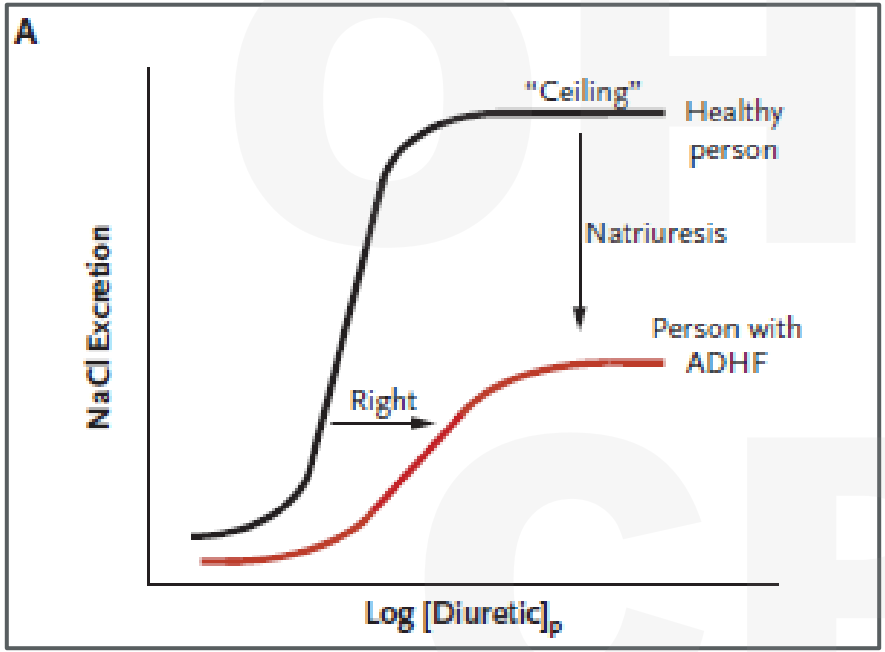
- Lots of rescue diuretic (metolazone, extra doses, etc)
- Significantly more fluid loss with high dose (4.9 L vs. 3.5 L)
- No change in length of stay or days alive out of hospital

Challenges with diuretic trials

- Limited funding/sponsorship
- HF patients are heterogenous
- Escalation of therapy = pseudo-crossover
- End-points
  - Weight/fluid loss?
  - Symptoms?
  - Re-admission/mortality (hard end-points)

Physiology > Evidence?

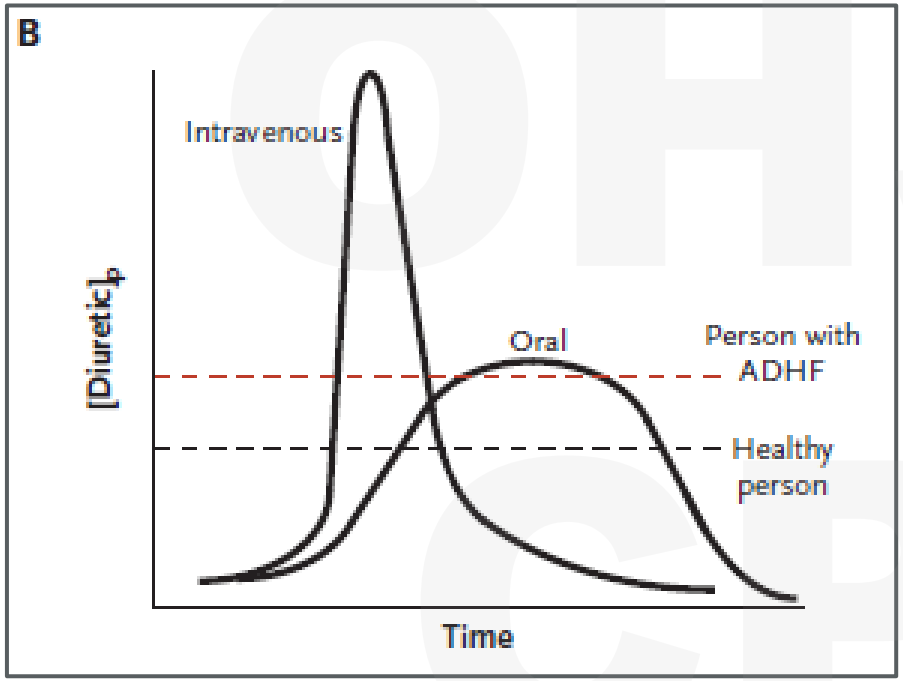
Diuretic physiology part 1



Find the right dose (did it work?)

Ellison DH, Felker GM, NEJM 2017

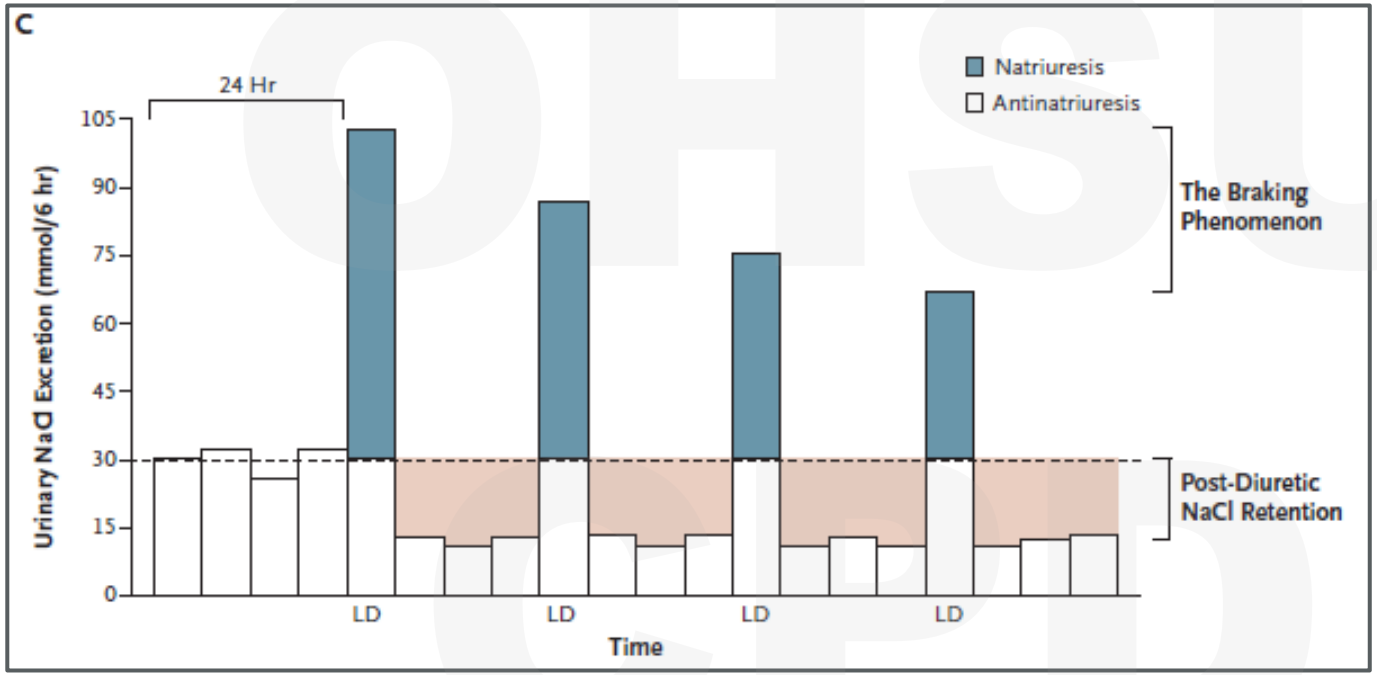
Diuretic physiology part 2



Get and stay above diuretic threshold

Ellison DH, Felker GM, NEJM 2017

Diuretic physiology part 3



Dosing frequency matters

Ellison DH, Felker GM, NEJM 2017

Beyond loop diuretics

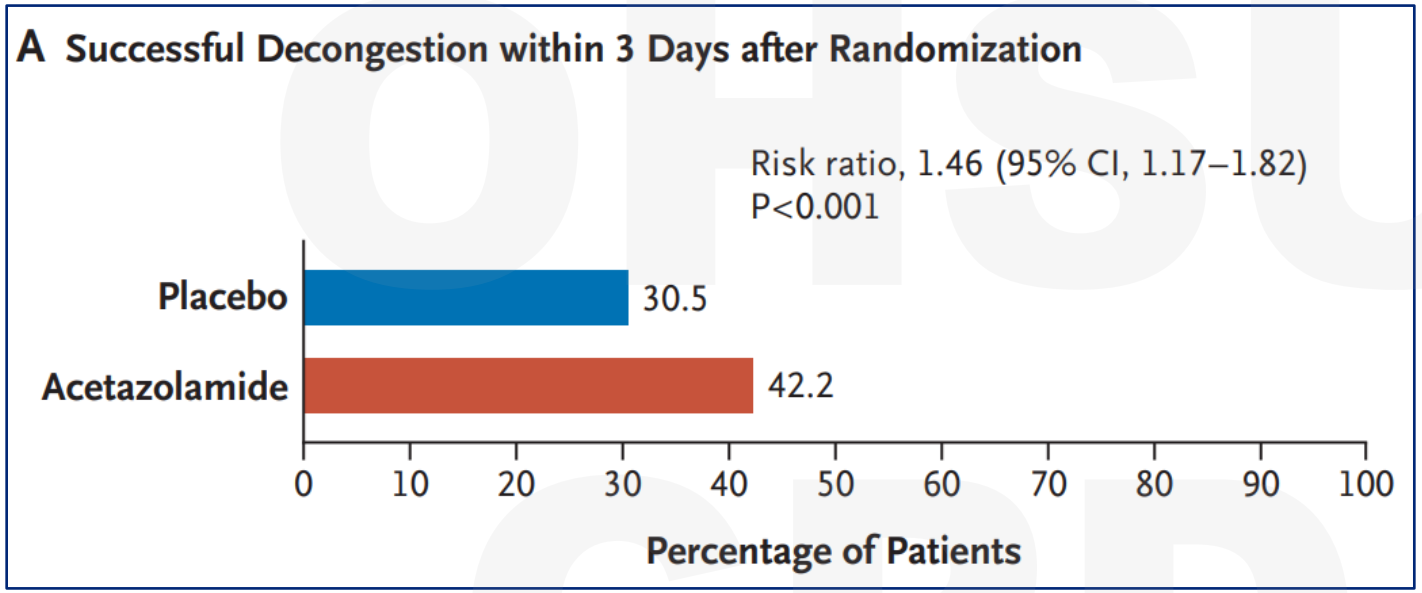
ORIGINAL ARTICLE

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, K. Tartaglia, F. Chenot, S. Moubayed, R. Dierckx, P. Blouard, P. Troisfontaines, D. Derthoo, W. Smolders, L. Bruckers, W. Droogne, J.M. Ter Maaten, K. Damman, J. Lassus, A. Mebazaa, G. Filippatos, F. Ruschitzka, and M. Dupont, for the ADVOR Study Group*

- HF patients treated with 2x home diuretic (transitioned to IV) randomized to acetzolamide vs. placebo
- Primary outcome: decongestion at 72 hours without need for escalation of diuretic

ADVOR outcomes



- No improvement in hospitalization or mortality (secondary end points)

Mullens, et al. NEJM 2022

Thiazide diuretics

CENTRAL ILLUSTRATION: The CLOROTIC Trial Results According to LVEF

Study Population

Randomized, double-blind, placebo-controlled clinical trial

- ✓ History of chronic heart failure
- ✓ Admission for acute decompensation
- ✓ Treatment with oral furosemide (80-240 mg/day)

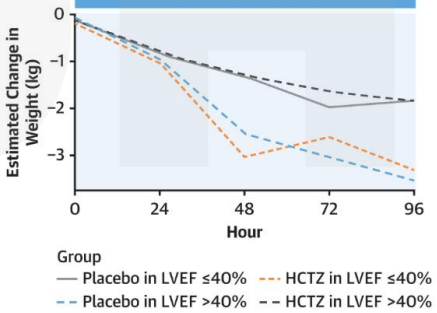
230 patients were randomized to 5 days oral treatment with hydrochlorothiazide or placebo

Hydrochlorothiazide dose adjusted to eGFR
>50 mL/min: 25 mg daily
20-50 mL/min: 50 mg daily
<20 mL/min: 100 mg daily

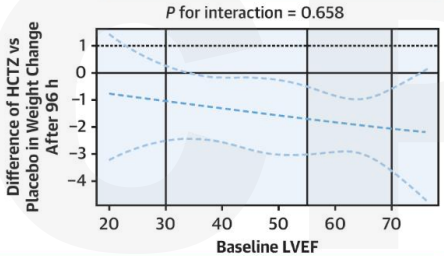
Median LVEF 55% (range 15%-86%)

HFrEF	HFmrEF	HFpEF
(LVEF ≤40%)	(LVEF 41%-49%)	(LVEF ≥50%)
n = 64 (28%)	n = 17 (7%)	n = 149 (65%)

Change in Weight at 72 and 96 Hours



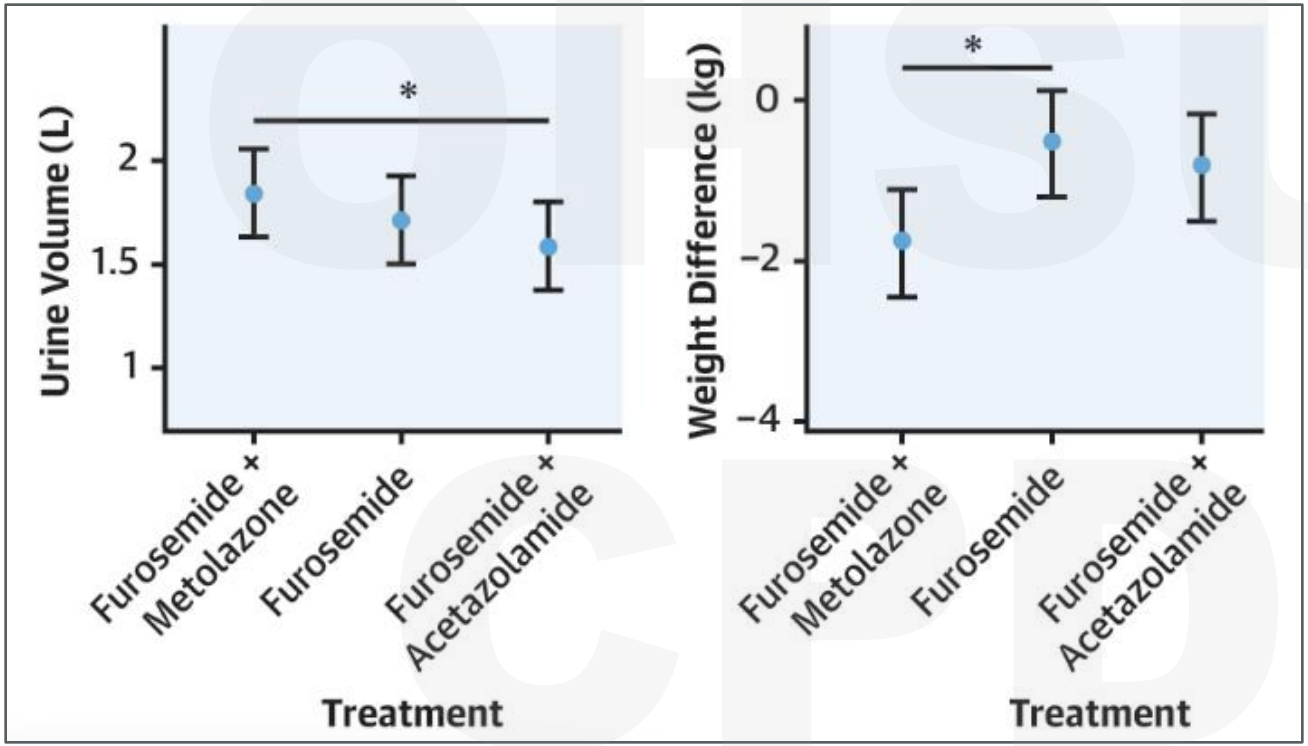
Difference in Weight (HCTZ vs Placebo) at 96 Hours



Adding oral HCTZ to intravenous furosemide improved the diuretic response in patients admitted due to AHF without treatment effect modification by baseline LVEF

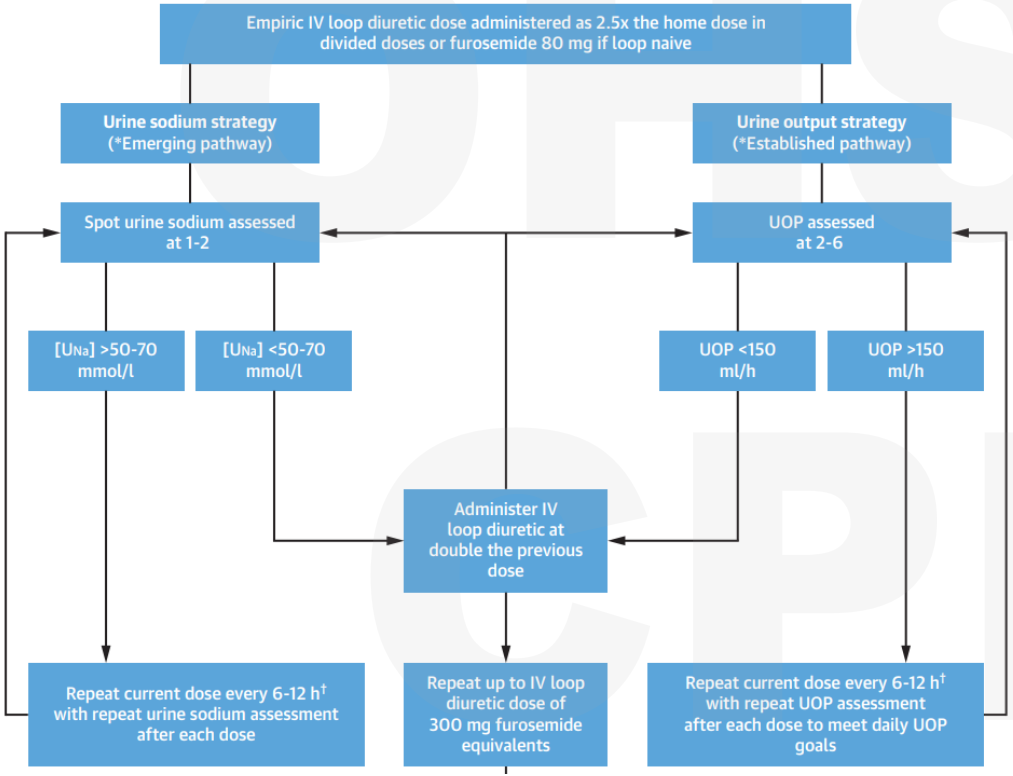
Sánchez-Marteles M, et al. JACC Heart Fail. 2024;12(10):1719-1730.

Diuretic regimens



Abbo, et al. JACC HF 2024

Diuretic algorithm



Failure to meet UOP or sodium goals at maximal loop diuretic doses

Combination diuretic blockade with loop diuretic:

First line: Add thiazide

Second line: Add additional diuretic agent which may include acetazolamide, amiloride, or diuretic doses of aldosterone antagonists

Felker, et al. JACC HF 2020

Euvolemic, now what?

- Furosemide will let you down when you need it most

TABLE 1. PHARMACOKINETICS OF DIURETIC DRUGS.*

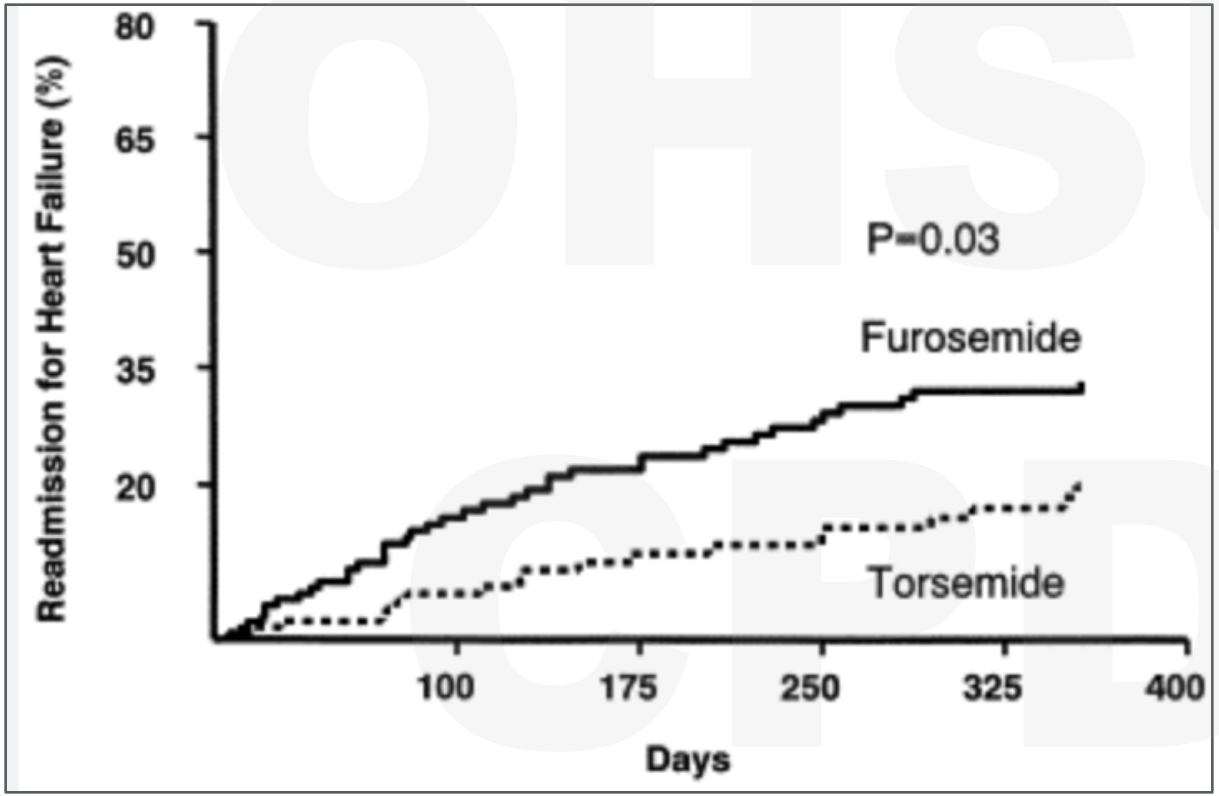
DIURETIC	ORAL BIOAVAILABILITY	ELIMINATION HALF-LIFE			
		NORMAL SUBJECTS	PATIENTS WITH RENAL INSUFFICIENCY	PATIENTS WITH CIRRHOSIS	PATIENTS WITH CONGESTIVE HEART FAILURE
	%	hr			
Loop					
Furosemide	10–100	1.5–2	2.8	2.5	2.7
Bumetanide	80–100	1	1.6	2.3	1.3
Torsemide	80–100	3–4	4–5	8	6
Thiazide					
Bendroflumethiazide	ND	2–5	ND	ND	ND
Chlorthalidone	64	24–55	ND	ND	ND
Chlorothiazide	30–50	1.5	ND	ND	ND
Hydrochlorothiazide	65–75	2.5	Increased	ND	ND
Hydroflumethiazide	73	6–25	ND	ND	6–28
Indapamide	93	15–25	ND	ND	ND
Polythiazide	ND	26	ND	ND	ND
Trichlormethiazide	ND	1–4	5–10	ND	ND
Distal					
Amiloride	Conflicting data	17–26	100	Negligible change	ND
Triamterene†	>80	2–5	Prolonged	No change	ND
Spironolactone	Conflicting data	1.5	No change	No change	ND
Active metabolites of spironolactone		>15	ND	ND	ND

*ND denotes not determined.

†Values are for the active metabolite.

Brater, NEJM 1998

Smoke

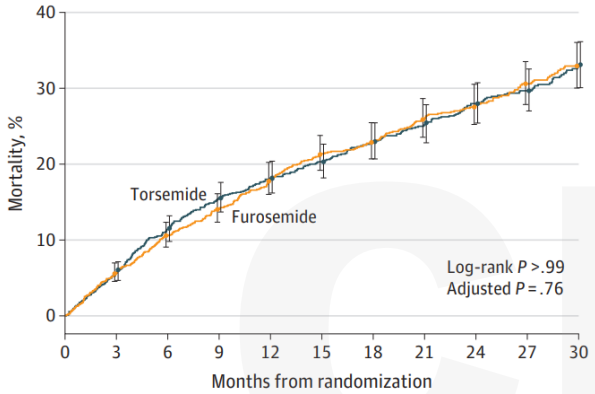


Murray, et al. AJM 2001

TRANSFORM-HF

- Pragmatic RCT of torsemide vs. furosemide in patients discharging from HF hospitalization

Figure 2. Primary Outcome of All-Cause Mortality



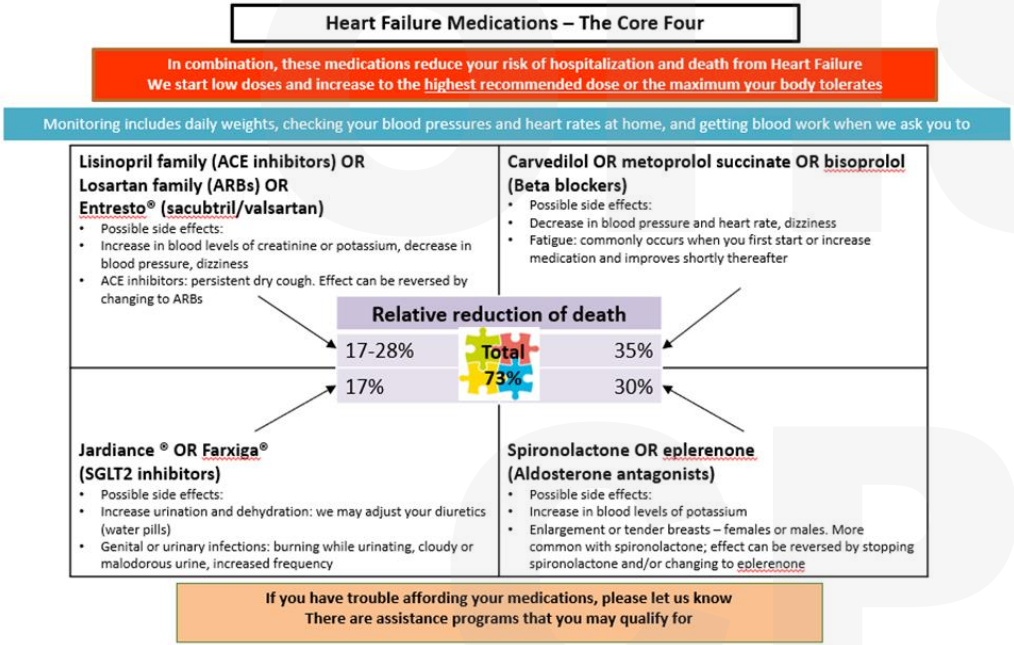
No. at risk

Torsemide	1431	1301	1135	1027	904	787	689	661	543	434	317
Furosemide	1428	1295	1151	1036	897	782	707	658	542	428	317

The cumulative incidence of the primary outcome in the 2 groups is shown. The whiskers represent 95% CIs at the months specified. Variables for the adjusted *P* value are listed in Table 2.

Mentz et al. JAMA 2023

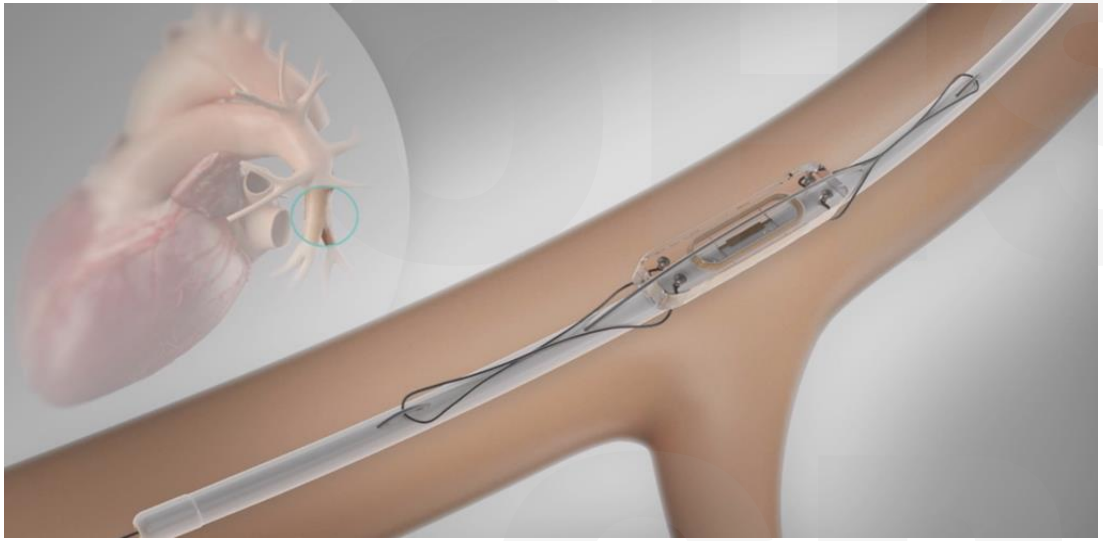
Don't forget GDMT

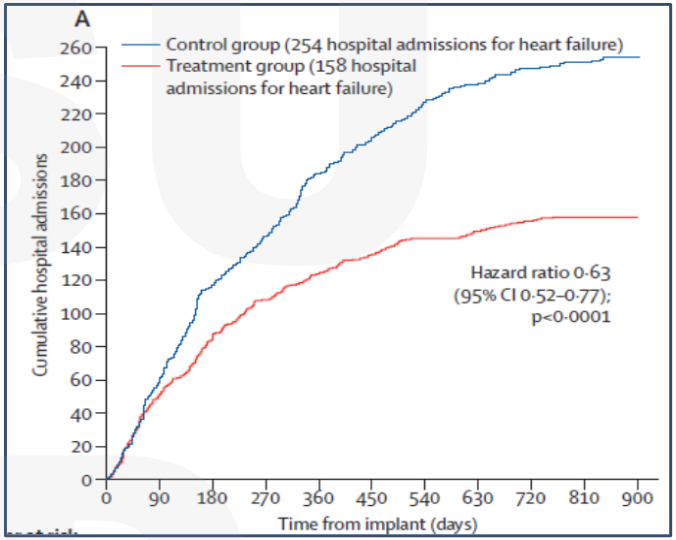


In HFrEF, decongestion is enhanced by ARNIs, MRA, SGLT2i

UNC REX HEALTHCARE

Guided diuretic – PA pressure monitoring





Abraham W, et al. Lancet 2011

Take aways*

- Go big or go home (2 to 2.5 x home dose converted to IV)
- Short feedback loop: dose every 6-12 hours
- If it doesn't work, increase the dose (target 150-250 mL/hr)
- If not responding to high dose loop (120-160 mg bolus or 20 mg/hr infusion), add thiazide or acetazolamide
- Oral furosemide will let you down when you need it most (try torsemide, dosed once daily)

Thank You

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