Nieuwste inzichten in behandeling van congestief hartfalen

Prof. dr. Wilfried Mullens

37th WCN-congres

New Frontiers

Nieuwste inzichten in behandeling van congestief hartfalen

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President-Elect HFA

November 29, 2024

Declaration of interest

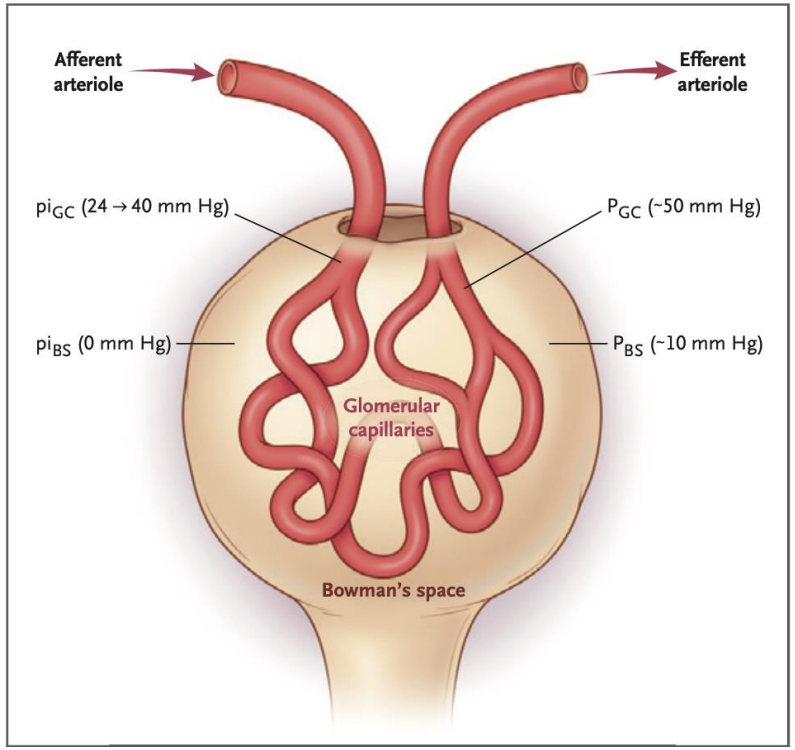
- Speaker fees to independent Hospital / University Fund

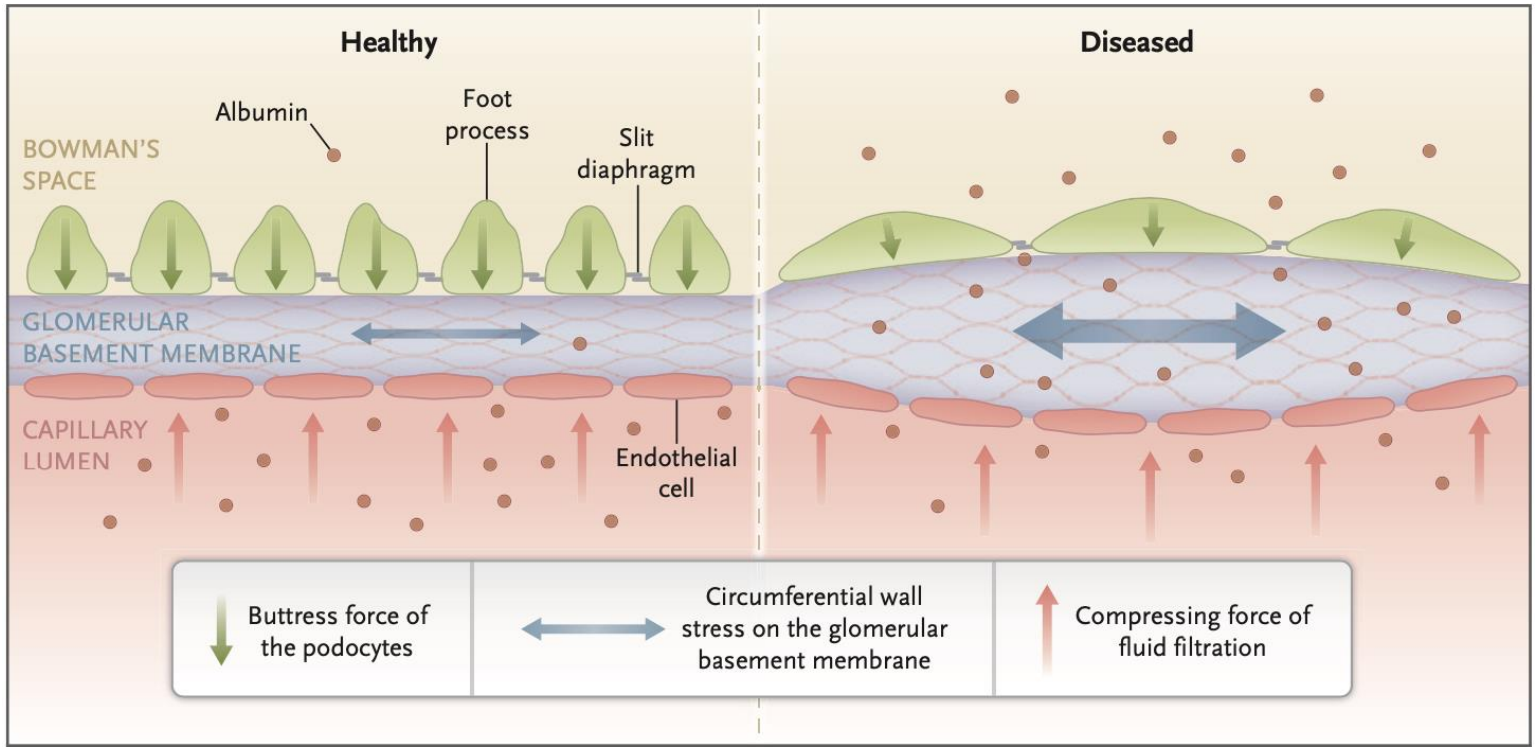
- Will (try to) explain what you should do in case of diuretic resistance and/or WRF….
  which is mostly reflecting ‘normal’ physiological response to HF

Conclusions

1. Renal function ≠ GFR
2. CKD is very prevalent and related to adverse outcomes
3. Certain agents delay the progression of CKD
4. Diuretic resistance / WRF is a normal physiological response
5. Do NOT stop decongestion / GDMT if WRF occurs

Single nephron GFR depending on integrity of podocytes and intraglomerular Starling pressure



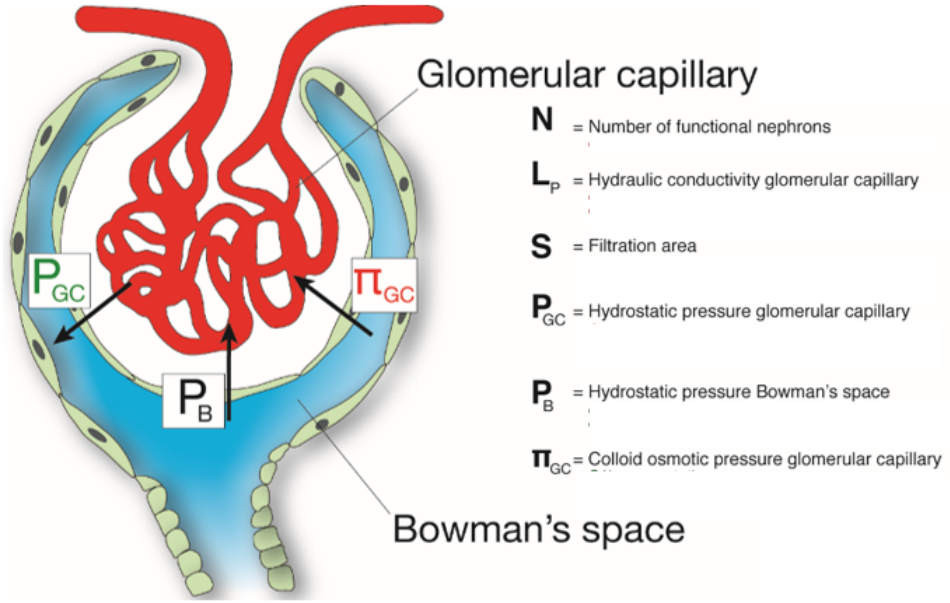


Benzing T et al, N Engl J Med 2021;384:1437-46.

RENAL FUNCTION

Glomerular filtration rate (GFR)

$$GFR = N \times L_P \times S \times (P_{GC} - P_B - \pi_{GC})$$



N = Number of functional nephrons

L_P = Hydraulic conductivity glomerular capillary

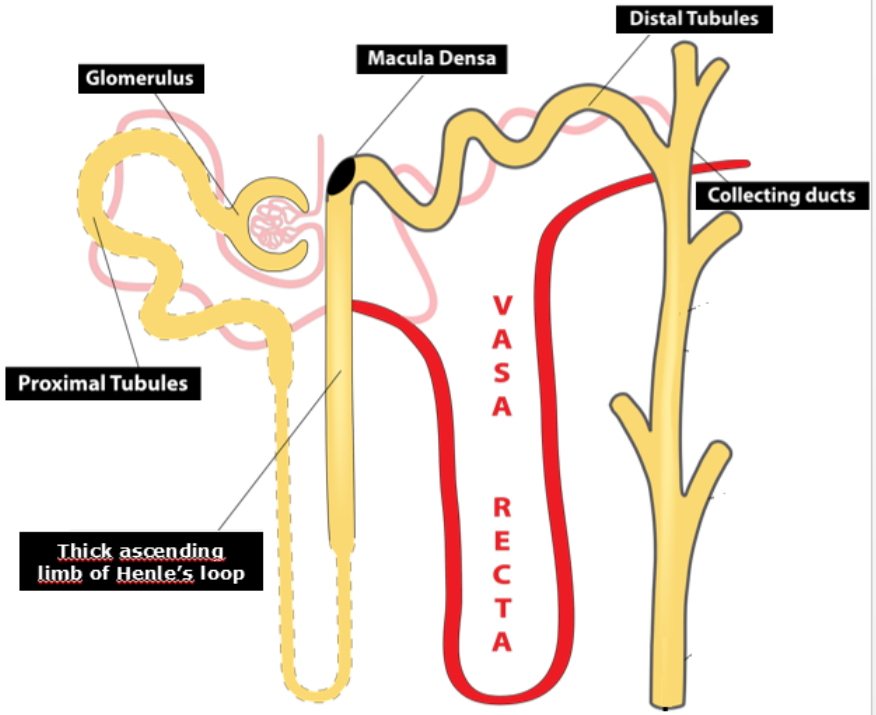
S = Filtration area

P_{GC} = Hydrostatic pressure glomerular capillary

P_B = Hydrostatic pressure Bowman's space

π_{GC} = Colloid osmotic pressure glomerular capillary

Tubular function

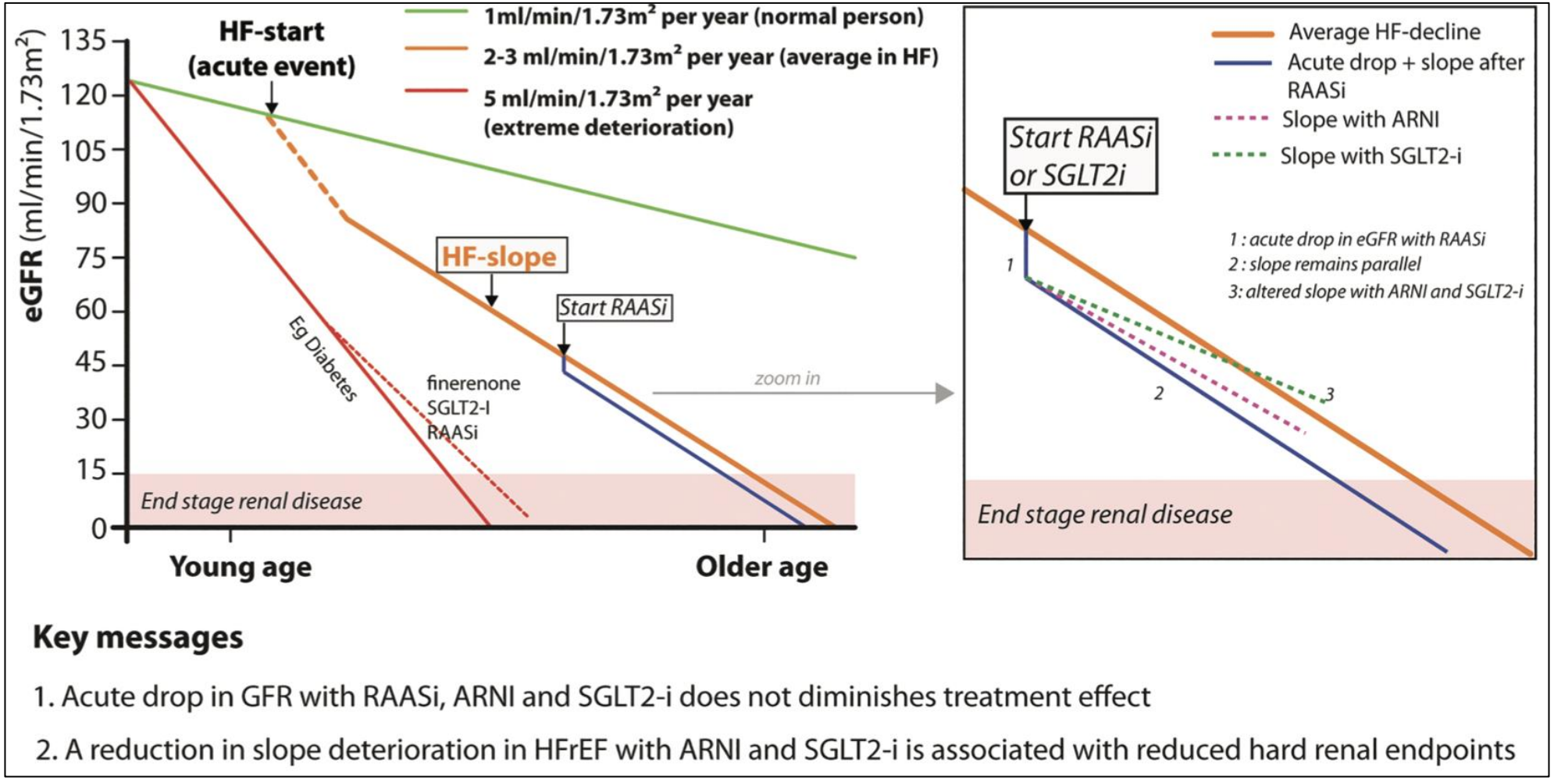


CLEARANCE

HOMEOSTASIS

Verbrugge F. Eur J Heart Fail. 2014;16:133-42
Mullens W, Eur J Heart Fail 2020; 22:584-603
Benzing T et al, N Engl J Med 2021;384:1437-46

CKD (eGFR < 60) affects > 50 % of HF patients + stronger predictor than LVEF



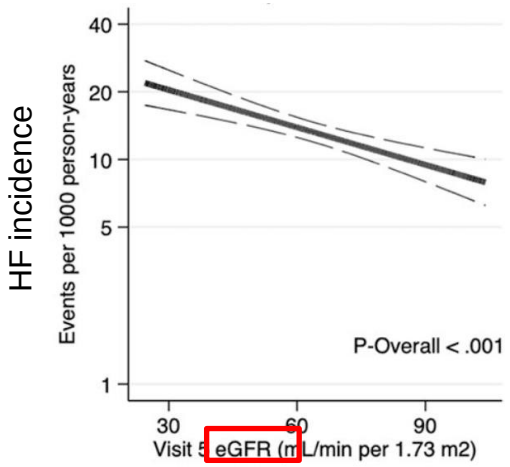
Key messages

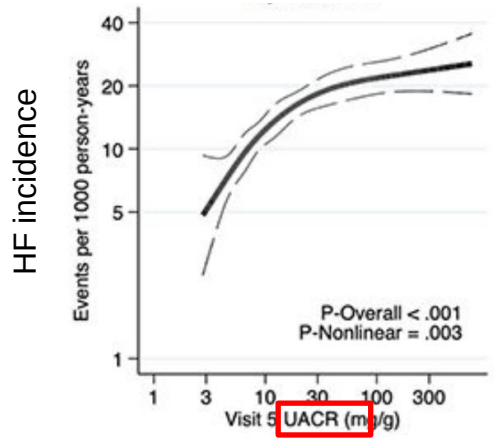
1. Acute drop in GFR with RAASi, ARNI and SGLT2-i does not diminishes treatment effect
2. A reduction in slope deterioration in HFrEF with ARNI and SGLT2-i is associated with reduced hard renal endpoints

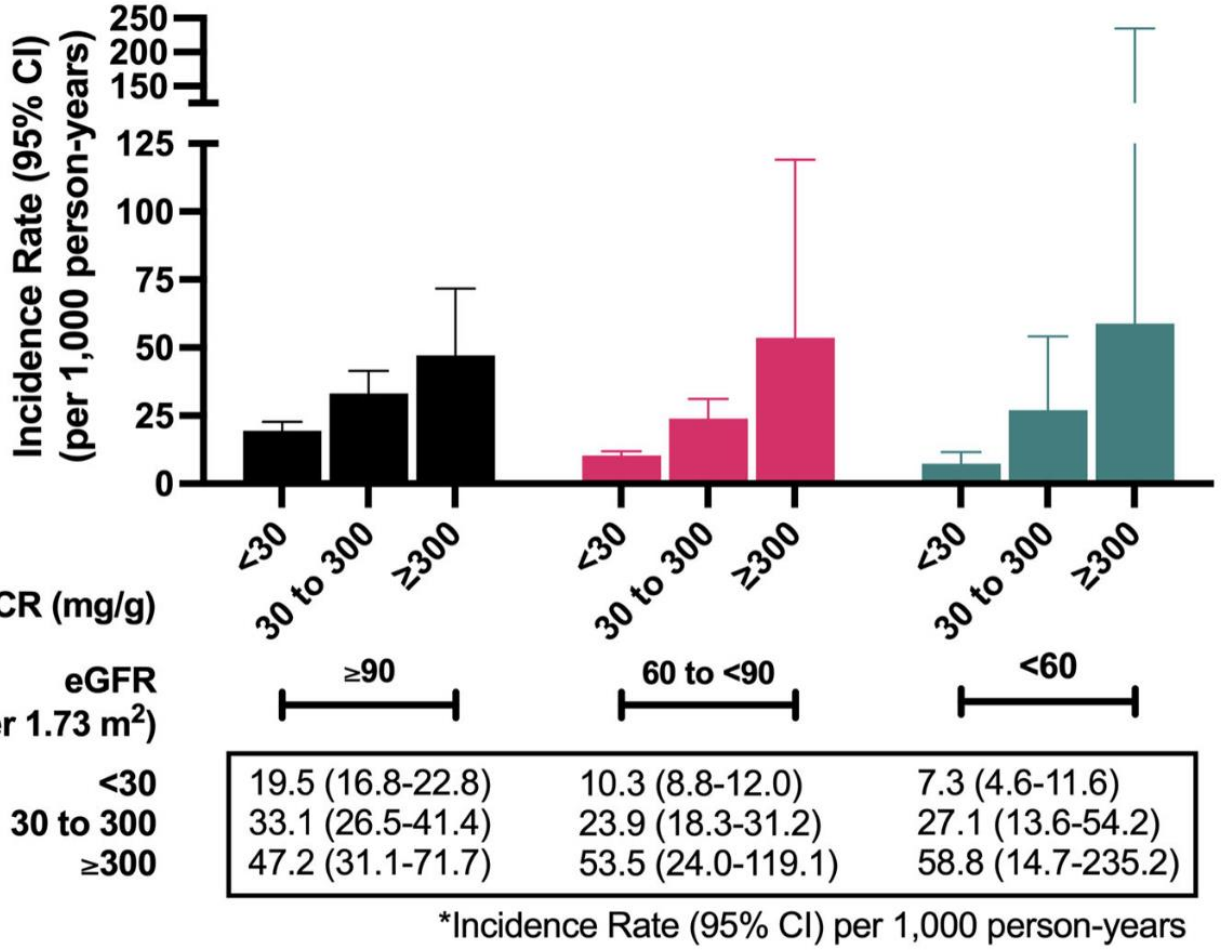
Mullens W, Eur J Heart Fail 2020; 22:584-603
Mullens W, Eur J Heart Fail 2022; 24:603-619.

Correlation between eGFR, UACR and HF

ARIC Study - Atherosclerosis Risk in Communities study (5170 pnts)







Buckley L et al, JACC Heart Fail 2023;11:523–537

GDMT in relation to CKD

Drug	Evidence across GFR strata according to baseline eGFR enrolment criteria	Acute drop GFR	Impact on GFR slope in HF trial	CKD treatment interaction	Treatment effect with CKD
	ESKD 15–30 30–60 >60				
ACE-I/ARB	Moderate evidence if dialysis, weak evidence if not on dialysis	Yes	No (beneficial effect of around 1–2 ml/min/1.73 m^2 per year in CKD trials)	No	Relative benefit: ~ Absolute benefit: ↑
Beta-blockers		No	No	Yes (potentially but some conflicting results)	Relative benefit: ~ Absolute benefit: ↑
MRA		Yes	No	No	Relative benefit: ~ Absolute benefit: ↑
ARNI		Yes	Yes (around 0.5 ml/min/1.73 m^2 per year)	No	Relative benefit: ~ Absolute benefit: ↑
SGLT2-i	>20	Yes	Yes (around 1–2 ml/min/1.73 m^2 per year)	No	Relative benefit: ~ Absolute benefit: ↑

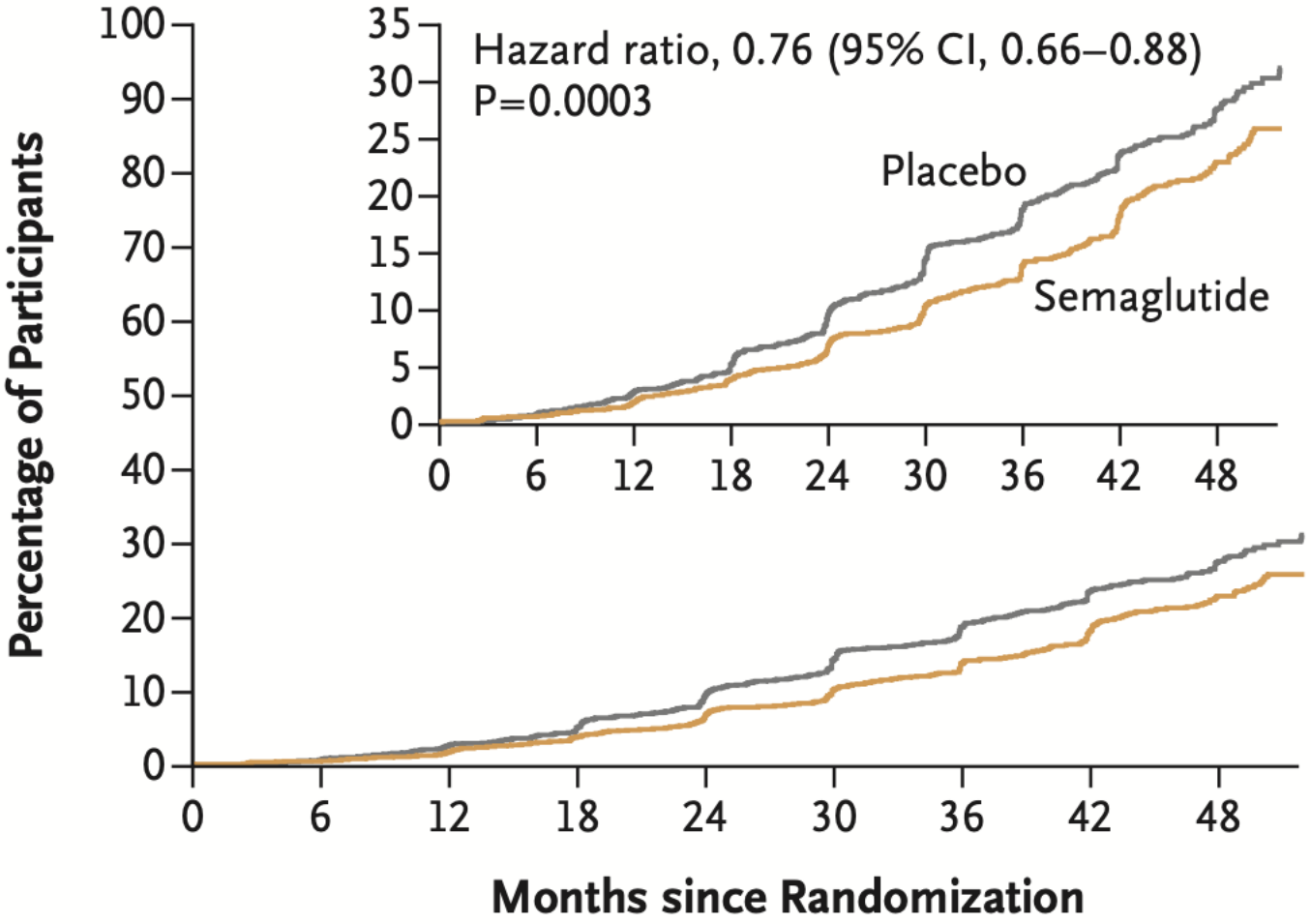
GLP1 (Semaglutide) in FLOW RCT (CKD + DM), 24% RR in progression CKD / CV death

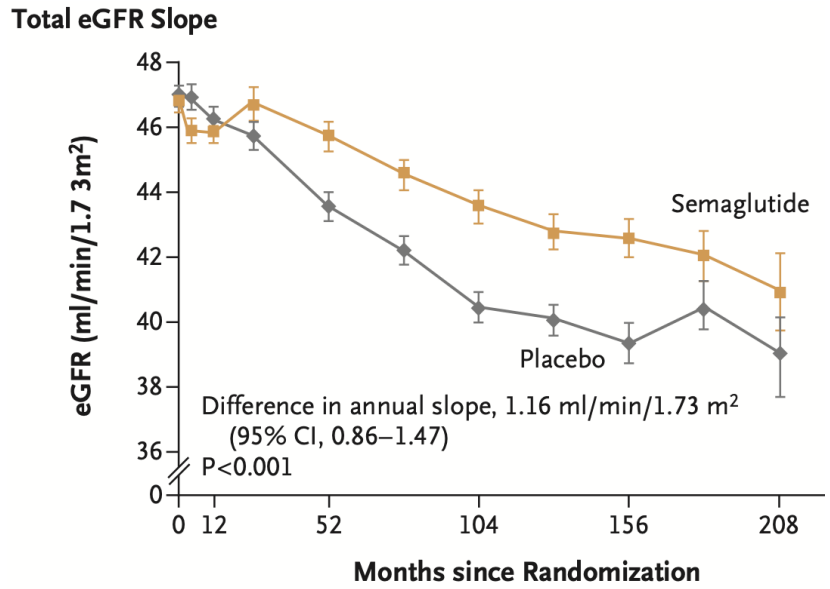
Mullens W, Martens P. Eur J Heart Fail 2022;24:603-619.

Semaglutide in CKD (FLOW)

Type 2 DM
eGFR 50-75 – uACR > 300
eGFR 25-50 – uACR > 100
1 mg sema / w vs placebo

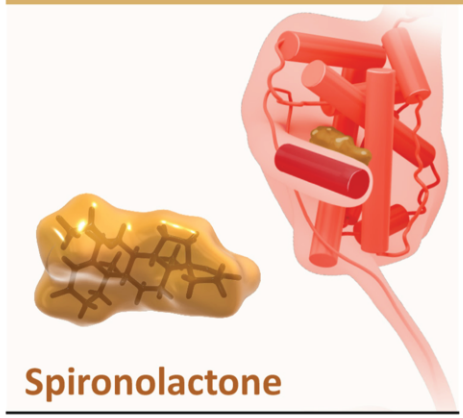
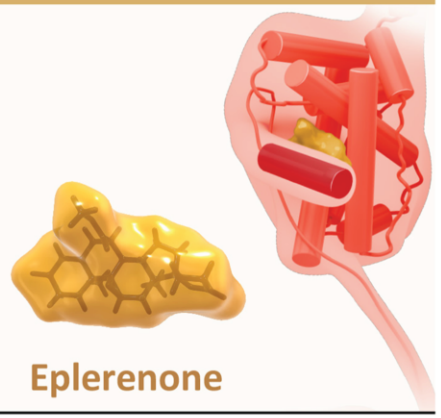
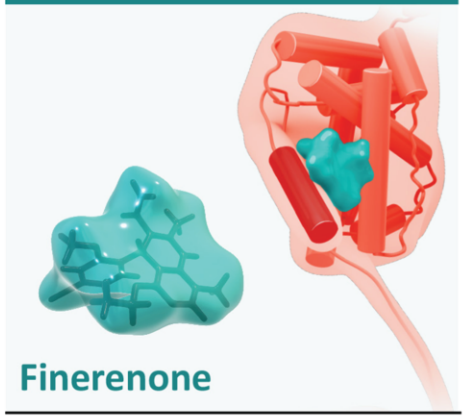
First major kidney disease events
kidney failure / > 50% reduction in the eGFR / CV death





Perkovich V. N Engl J Med 2024;391(2):109-121.

Finerone, the new ‘stronger and more selective’ MRA on the block

	Steroidal MRAs		Finerenone
	 Spironolactone	 Eplerenone	 Finerenone
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (non-steroidal)
Potency to MR	+++	+	+++
Selectivity to MR	+	++	+++
CNS penetration	+	+	–
Sexual side effects	++	(+)	–
Half-life	>20 h**	4–6 h**	2–3 h*
Active metabolites	++	–	–
Effect on BP	+++	++	+

Kintscher U et al. Br J Pharmacol 2022 Jul;179(13):3220-3234.

Recommendations	Class[a]	Level[b]
In patients with T2DM and CKD,[c] SGLT2 inhibitors (dapagliflozin or empagliflozin) are recommended to reduce the risk of HF hospitalization or CV death.[5,7,35]	I	A
In patients with T2DM and CKD,[c] finerenone is recommended to reduce the risk of HF hospitalization.[10,11,34,40]	I	A

FIDELIO-DKD
FIGARO-DKD

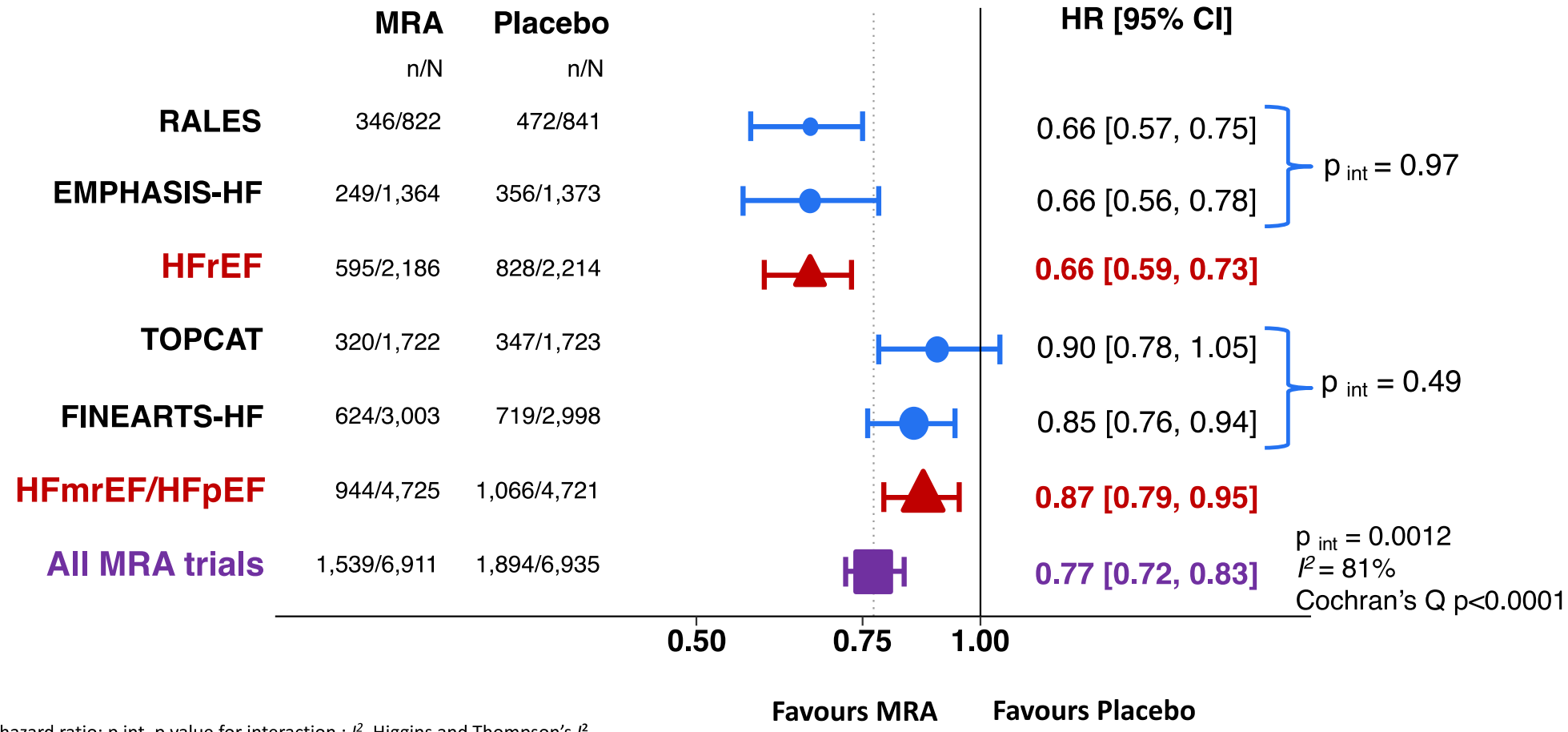
Mc Donagh T et al. Eur Heart J 2023 ;44(37):3627-3639

Mineralocorticoid receptor antagonists in heart failure

Key trial characteristics	RALES	EMPHASIS-HF	TOPCAT	FINEARTS-HF
Investigational drug	spironolactone	eplerenone	spironolactone	finerenone
Number of patients, sites and countries	1663 patients at 195 sites in 15 countries	2737 patients at 278 sites in 29 countries	3445 participants at 233 sites in 6 countries	6001 patients at 654 sites in 37 countries
Key inclusion criteria	Ejection fraction ≤35%	Ejection fraction ≤30% (or, if >30 to 35%, a QRS duration of >130 msec on electrocardiography)	Ejection fraction ≥45%	Ejection fraction ≥40% including improved ejection fraction

Jhund P et al. ESC congress London 2024.

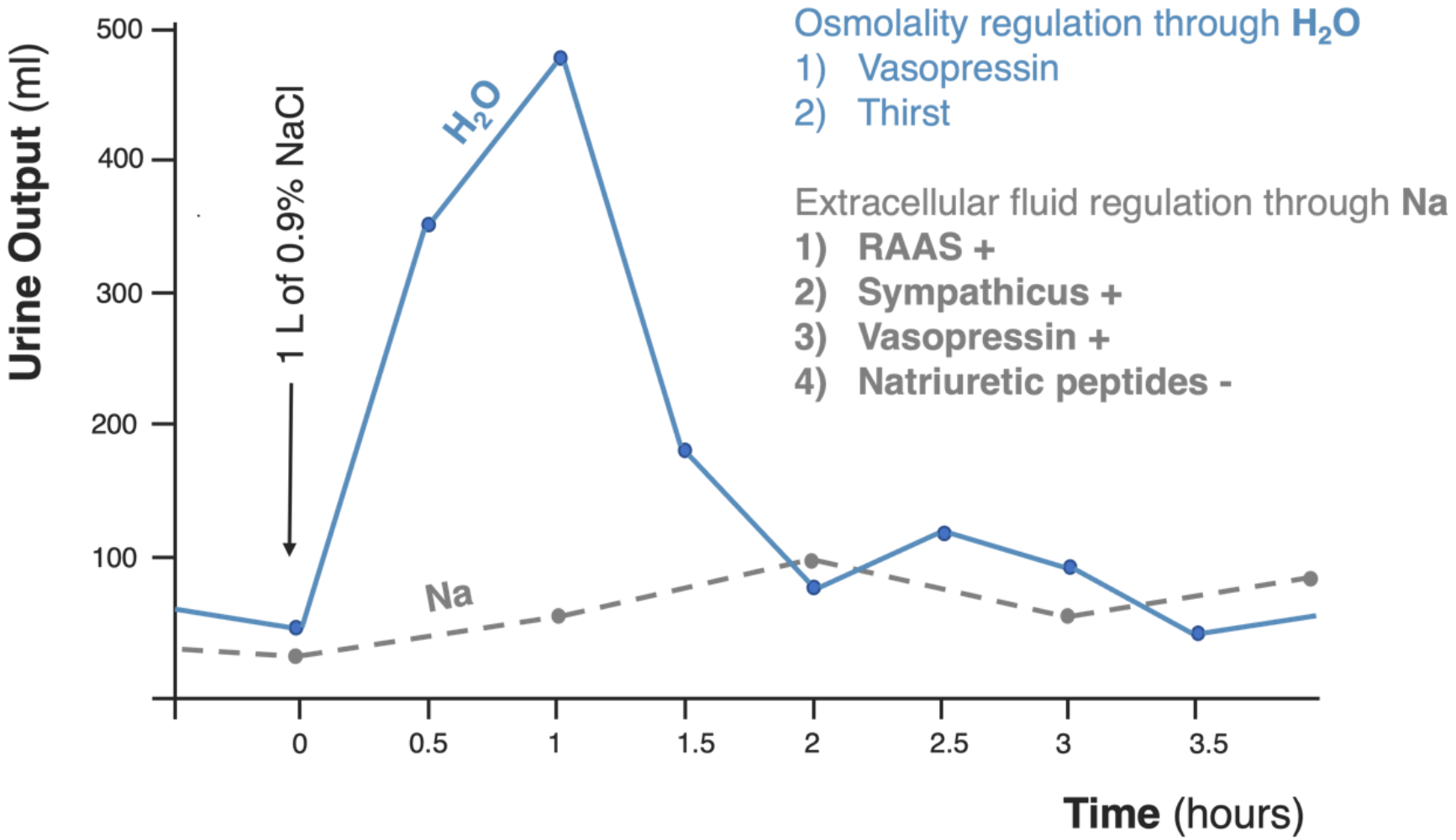
Mineralocorticoid receptor antagonists in heart failure: CV death / HFH



HR, hazard ratio; p int, p value for interaction ; I^2, Higgins and Thompson's I^2

Jhund P et al. Lancet 2024;404;1119-1131.

‘more difficult to loose sodium than water’

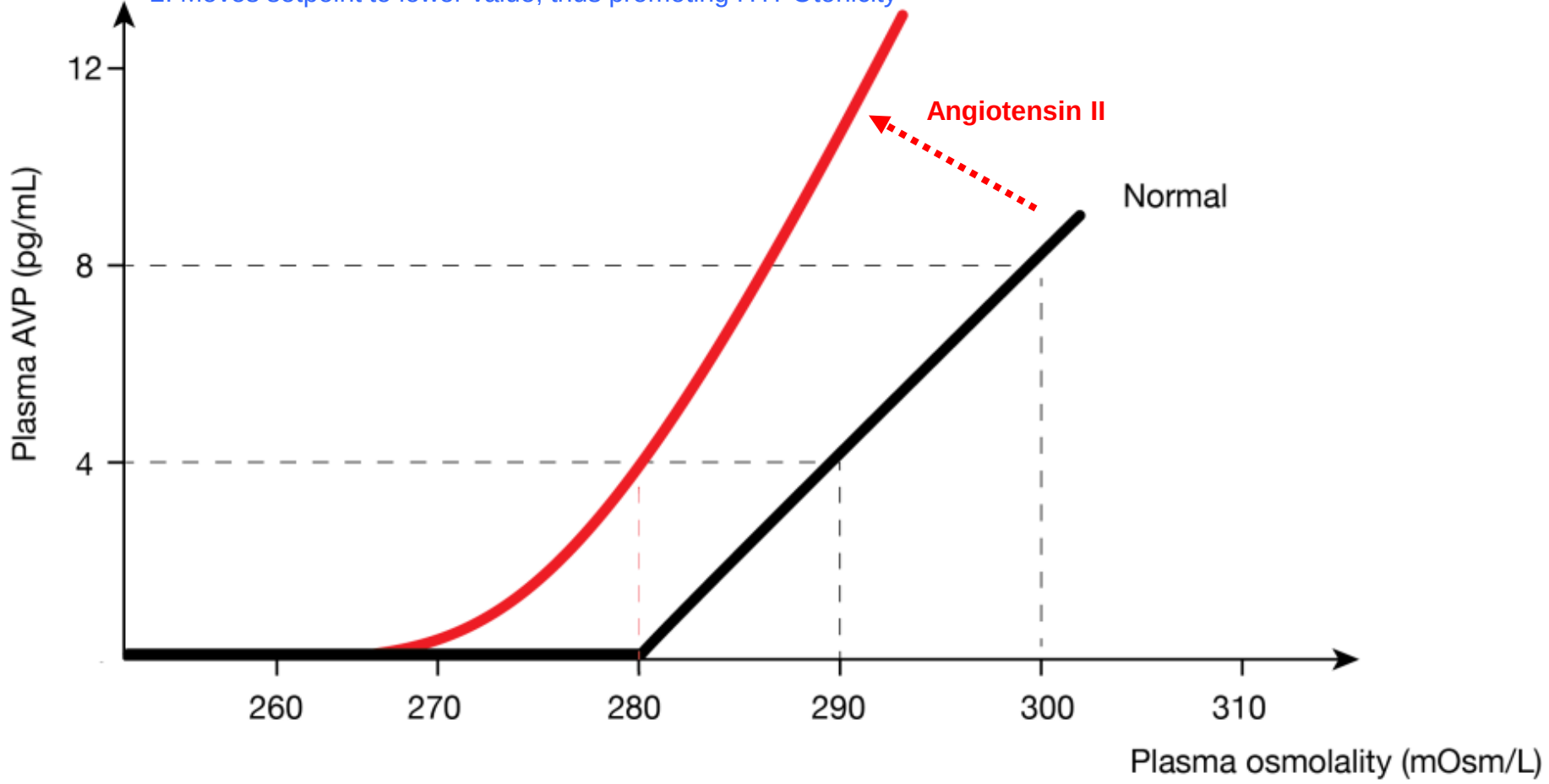


Mullens W, Damman K, Dhondt S et al. Eur J Heart Fail 2024.

Increased plasma release of AVP in advanced heart failure

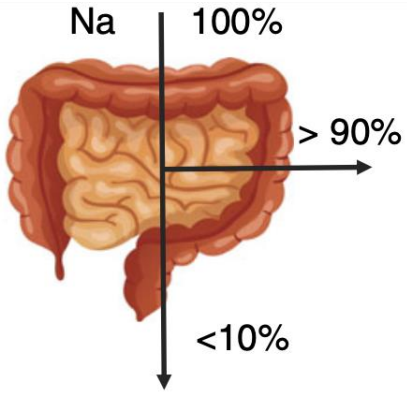
1. More AVP for any given osmolality

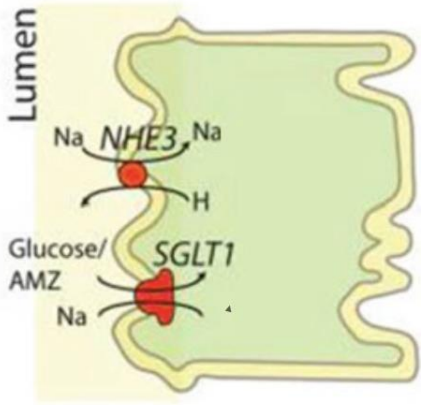
2. Moves setpoint to lower value, thus promoting HYPOtonicity



Verbrugge F, Mullens W. J Am Col Card 2015;65:480-92.

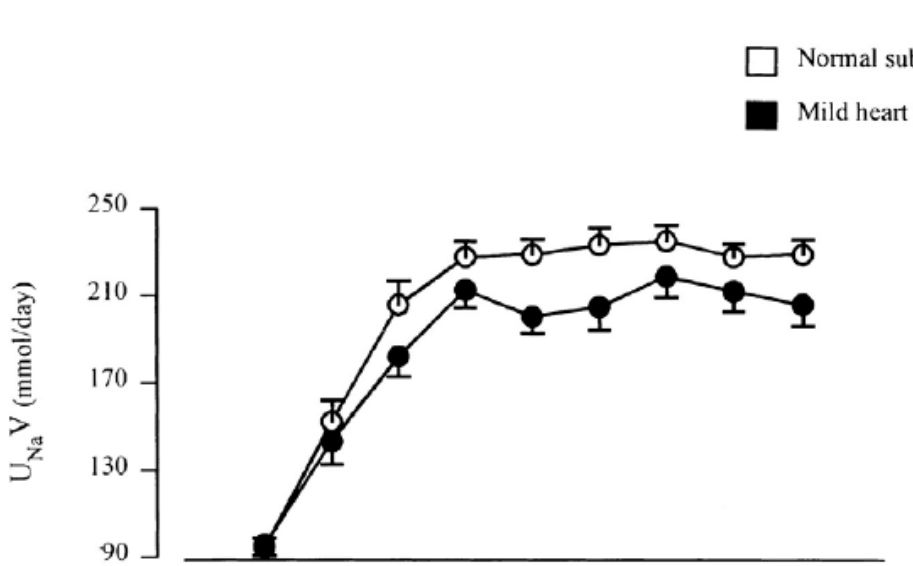
GI absorption of sodium is 100% in everybody (even without HF)



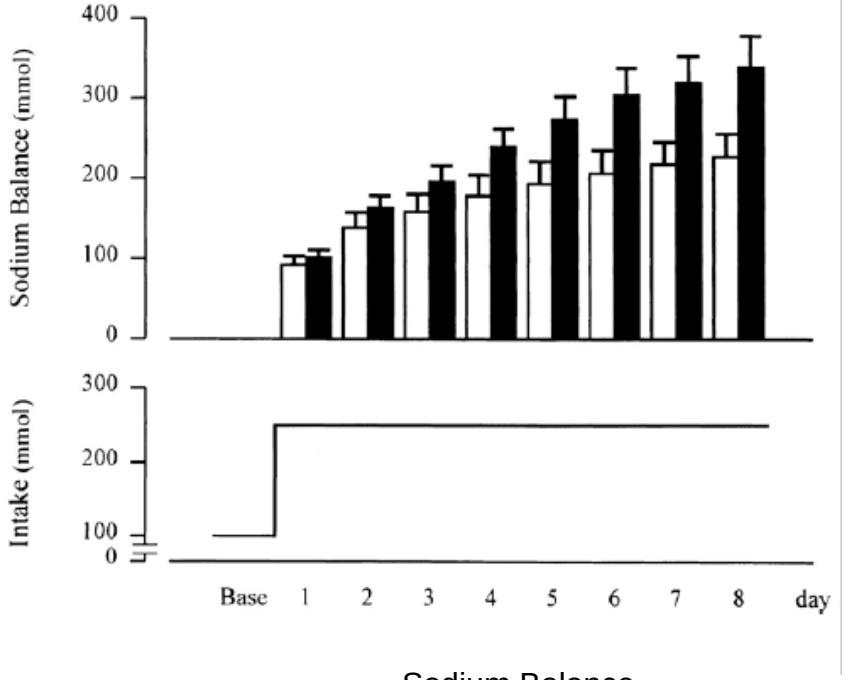


Mullens W, Damman K, Dhondt S et al. Eur J Heart Fail 2024.

Positive sodium balance - very fast



Natriuresis



Sodium Balance

Volpe M et al. Hypertension 1997

Journal of the American College of Cardiology

Published by Elsevier Inc.

EDITORIAL COMMENT

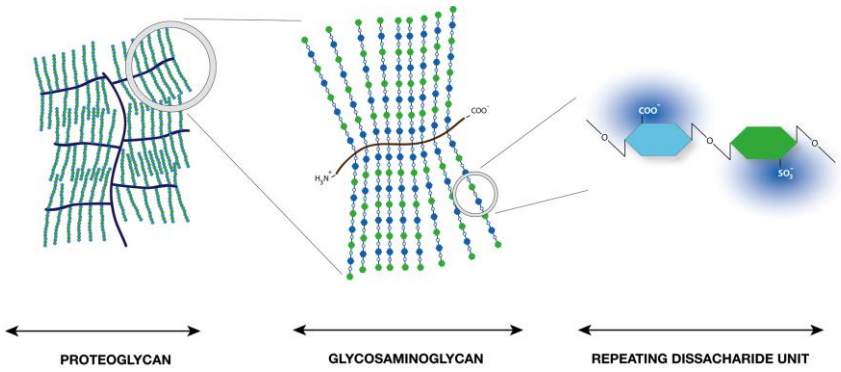
The Early Intertwining of the Heart and the Kidney Through an Impaired Natriuretic Response to Acute Volume Expansion*

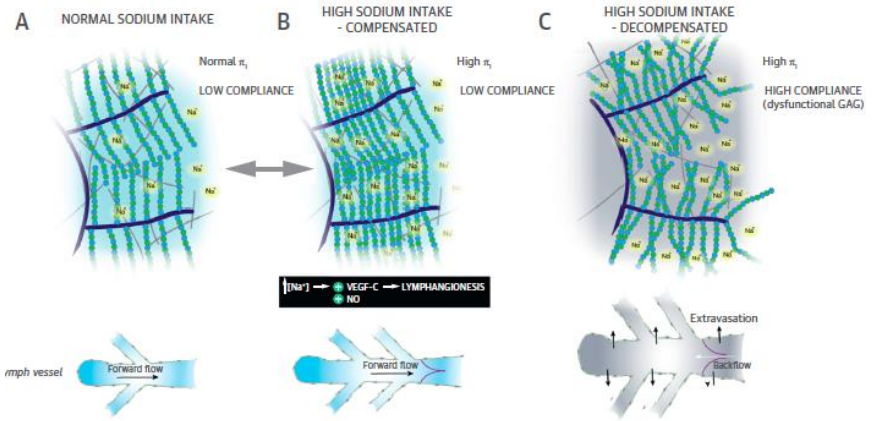
Wilfried Mullens, MD, PHD,†‡
W. H. Wilson Tang, MD§
Genk and Hasselt, Belgium; and Cleveland, Ohio

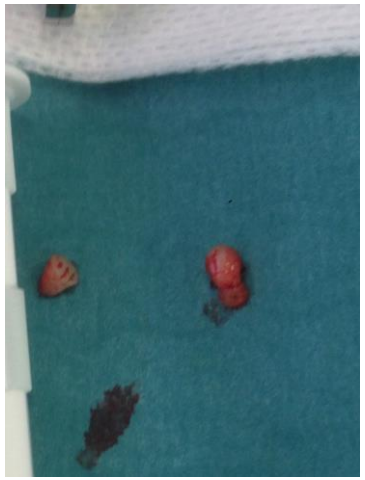
The problem of HF starts within the kidney

McKie P et al / Mullens W et al J Am Coll Card 2011.

Buffering of Sodium in Interstitium

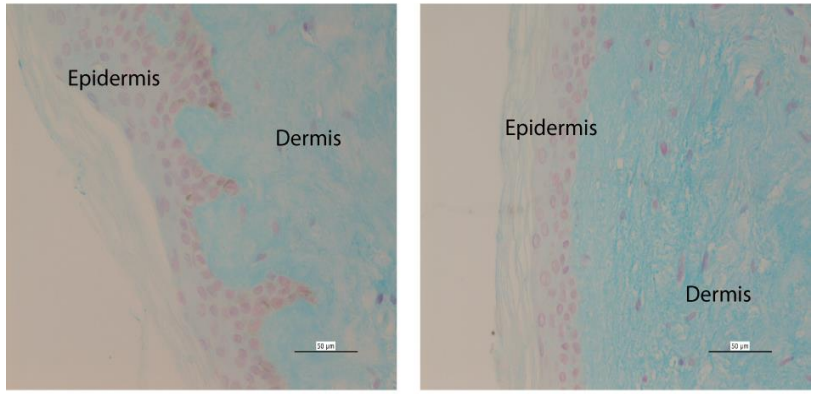




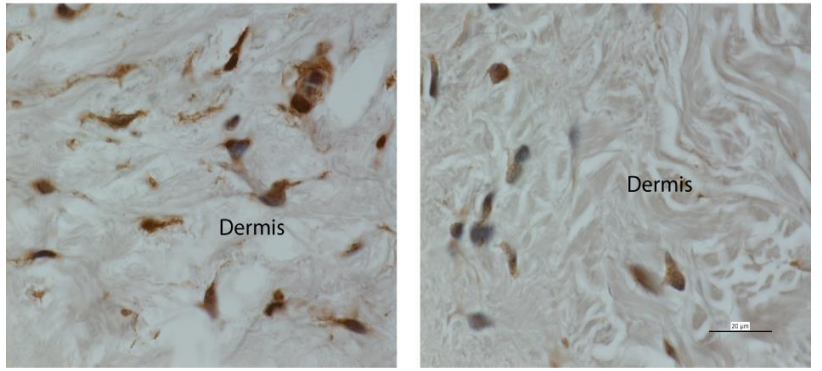


Healthy HFrEF

Alcian blue



Angiotensin II type 1 receptor



Nijst P, Mullens W. et al. Circ Heart Fail, 2018
Nijst P, Mullens W et al. J Am Coll Card 2015;65:378-88

Question; do HF patients tolerate sodium excess intake ?

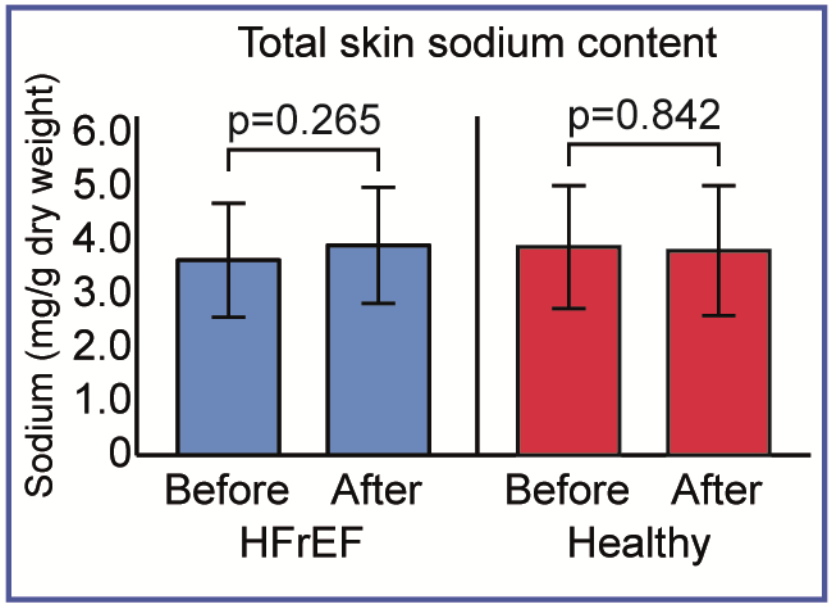
21 patients with HFrEF and 10 healthy controls

↓

4 weeks of daily 1.2 g sodium loading

	HFrEF	Healthy
Congestion		
Weight	=	=
NT-proBNP	=	=
Congestion score	=	=
Blood volume	=	=
Neurohormonal		
Renin	↓↓	=
Aldosterone	=	=
Renal		
Natriuresis	↑	↑↑
Diuresis	=	=

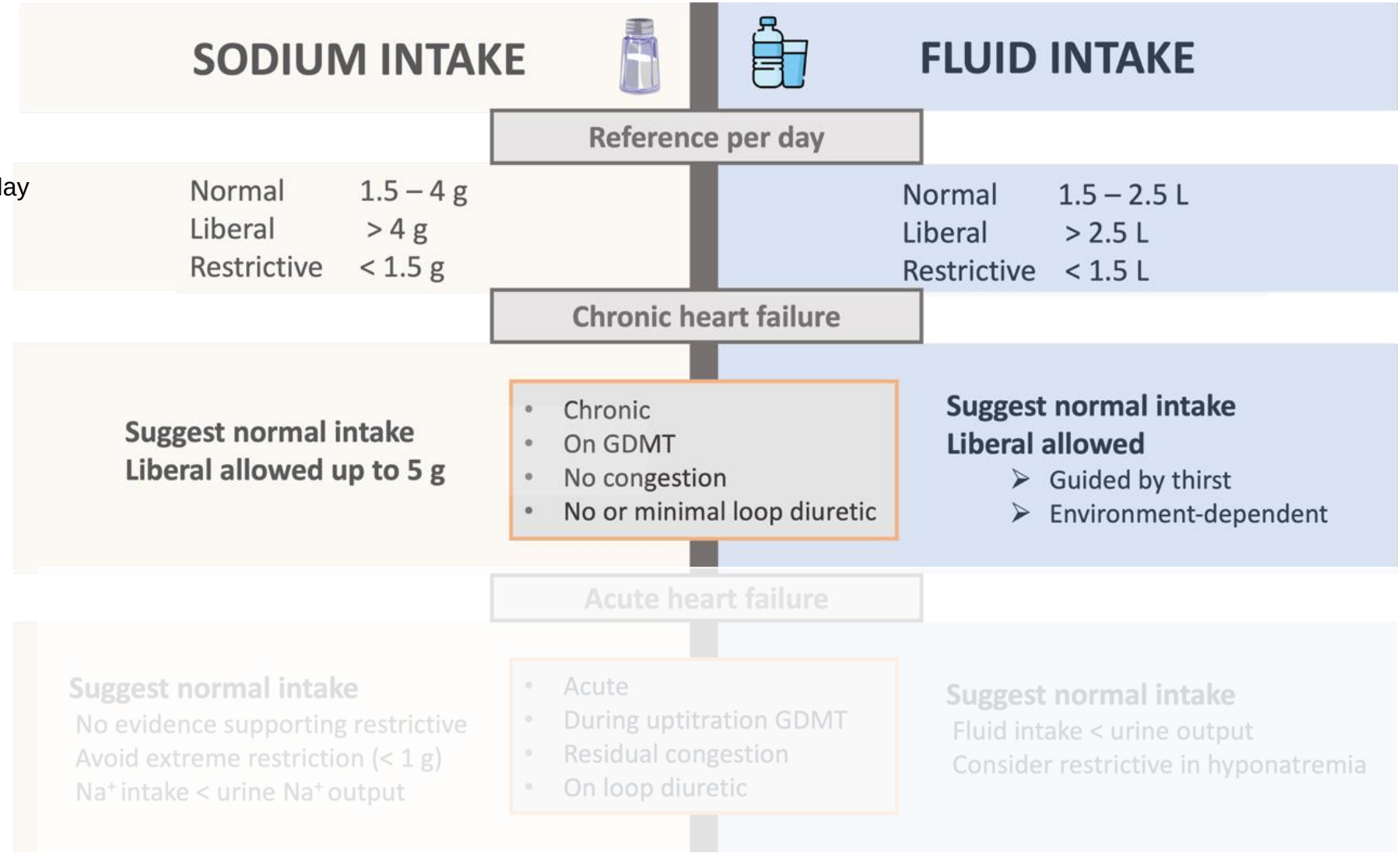
No change in skin sodium buffering



Dauw J, Mullens W. et al. Eur J Heart Fail 2024;26:616-624

Water and sodium recommendations ?

Equals 4-10 g NaCl
HFA: avoid > 5 g NaCl / day



Mullens W, Damman K, Dhondt S et al. Eur J Heart Fail 2024.

Question; why do HF pnts have a tendency to retain more sodium ?

Extracellular Volume = Na

Normal kidneys filter a tremendous amount of salt

GFR = 100 mL/min = 180 L/day

Plasma Na^+ = 142 mmol/L

25,560 mmol Na^+ filtered each day ~ > 1 kg sodium

Extracellular Volume = Na

Bad kidneys still filter a lot of salt

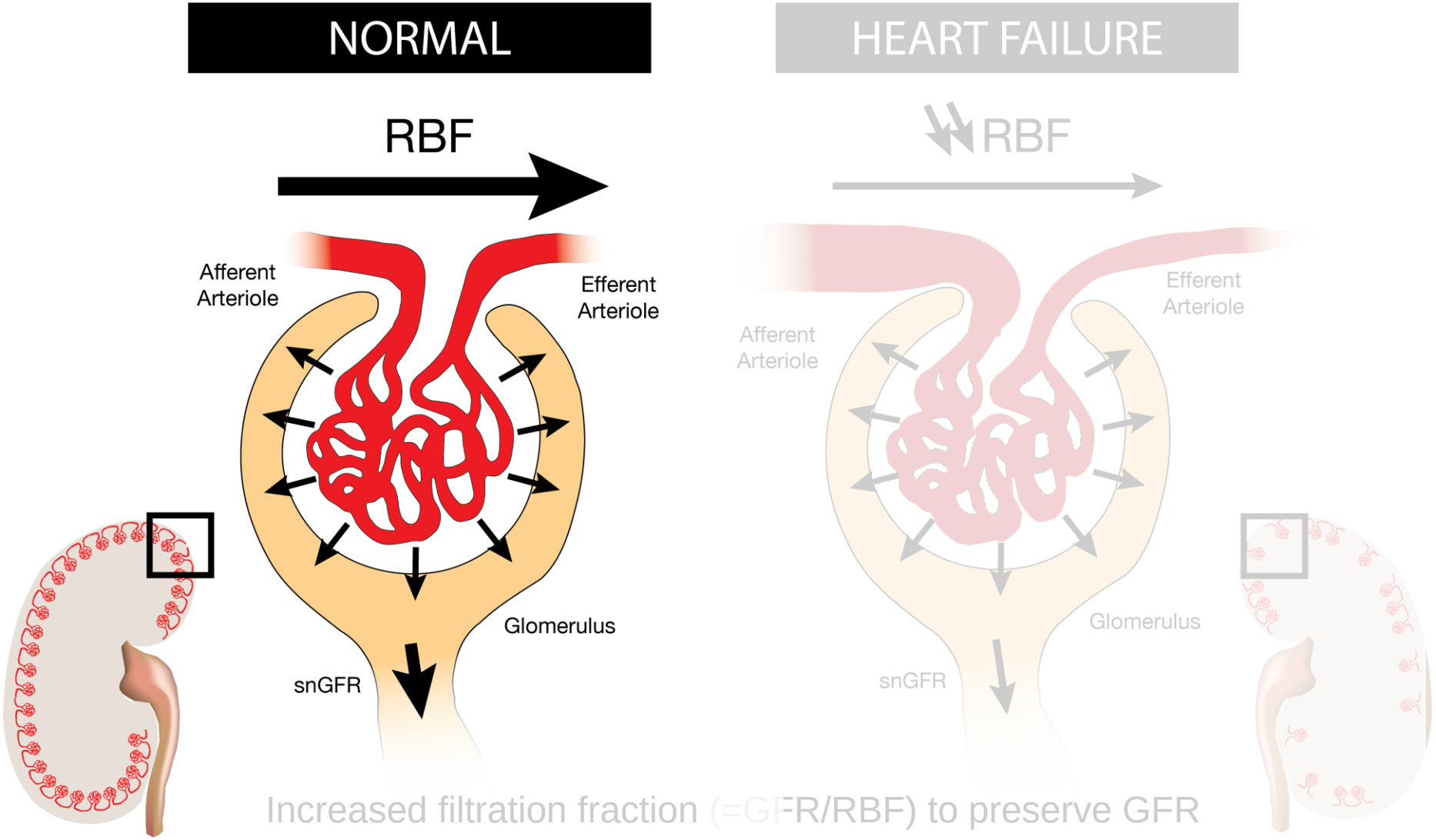
GFR = 10 mL/min = 20 L/day

Plasma Na^+ = 142 mmol/L

3500 mmol Na^+ filtered each day ~ 150 g sodium

Problem is not that the kidney filters too little sodium.....

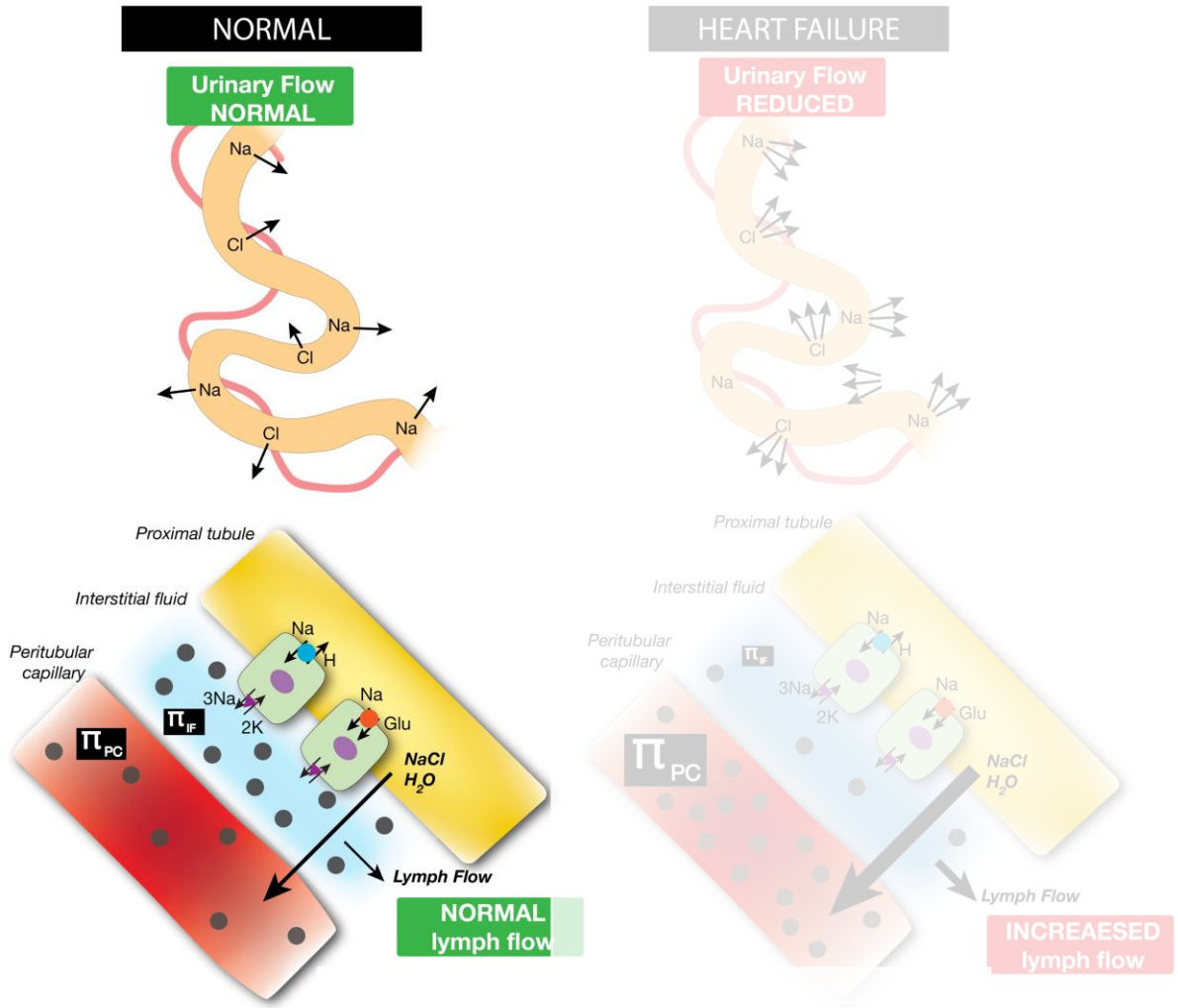
I: Glomerulus



Mullens W et al. Eur Heart J, 2017;38:1872-1882

II: Proximal Tubulus

Glomerulotubular Feedback

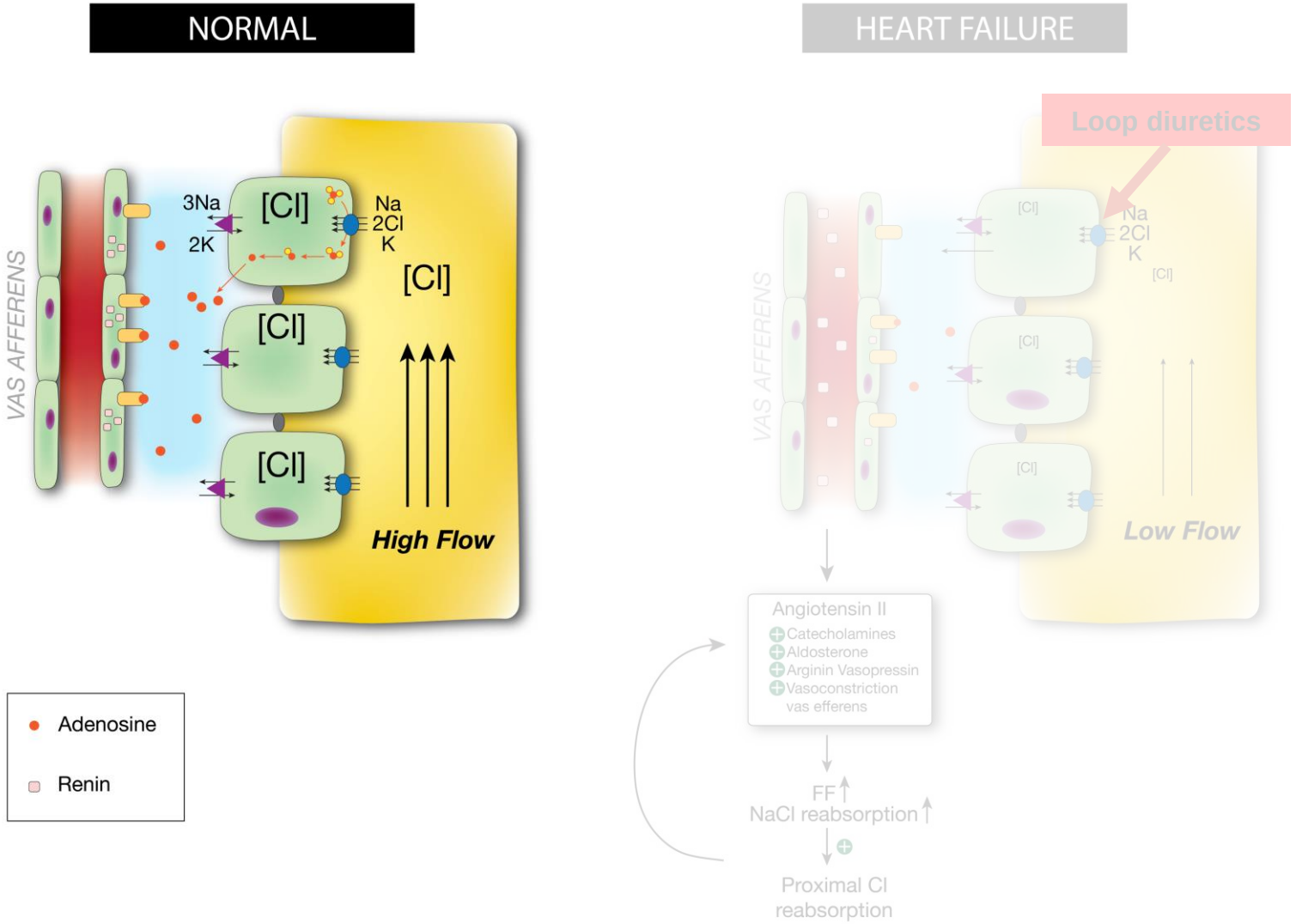


Increased Na reabsorption

Mullens W et al. Eur Heart J, 2017;38:1872-1882

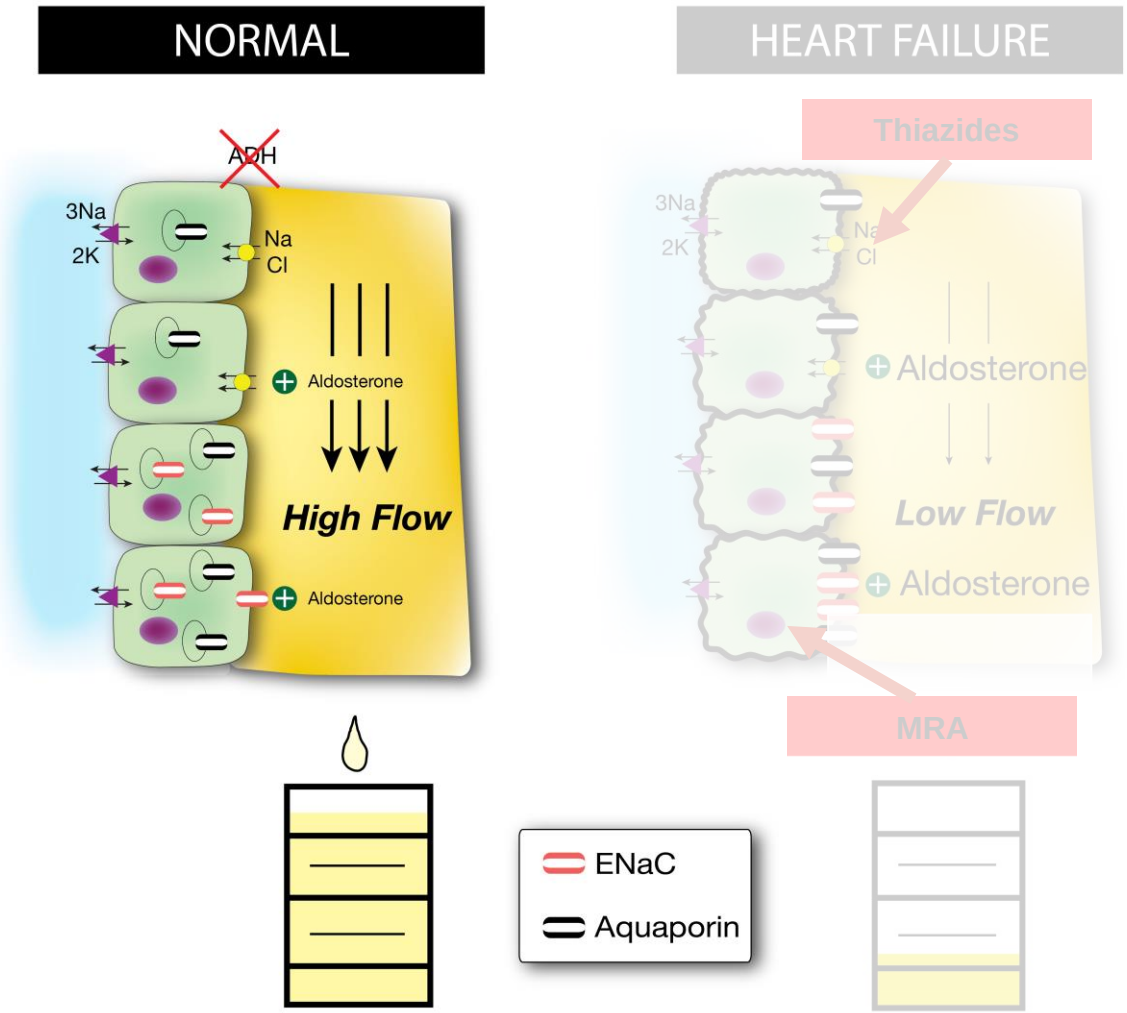
III: Loop of Henle - Macula Densa

Tubuloglomerular Feedback



Mullens W et al. Eur Heart J, 2017;38:1872-1882

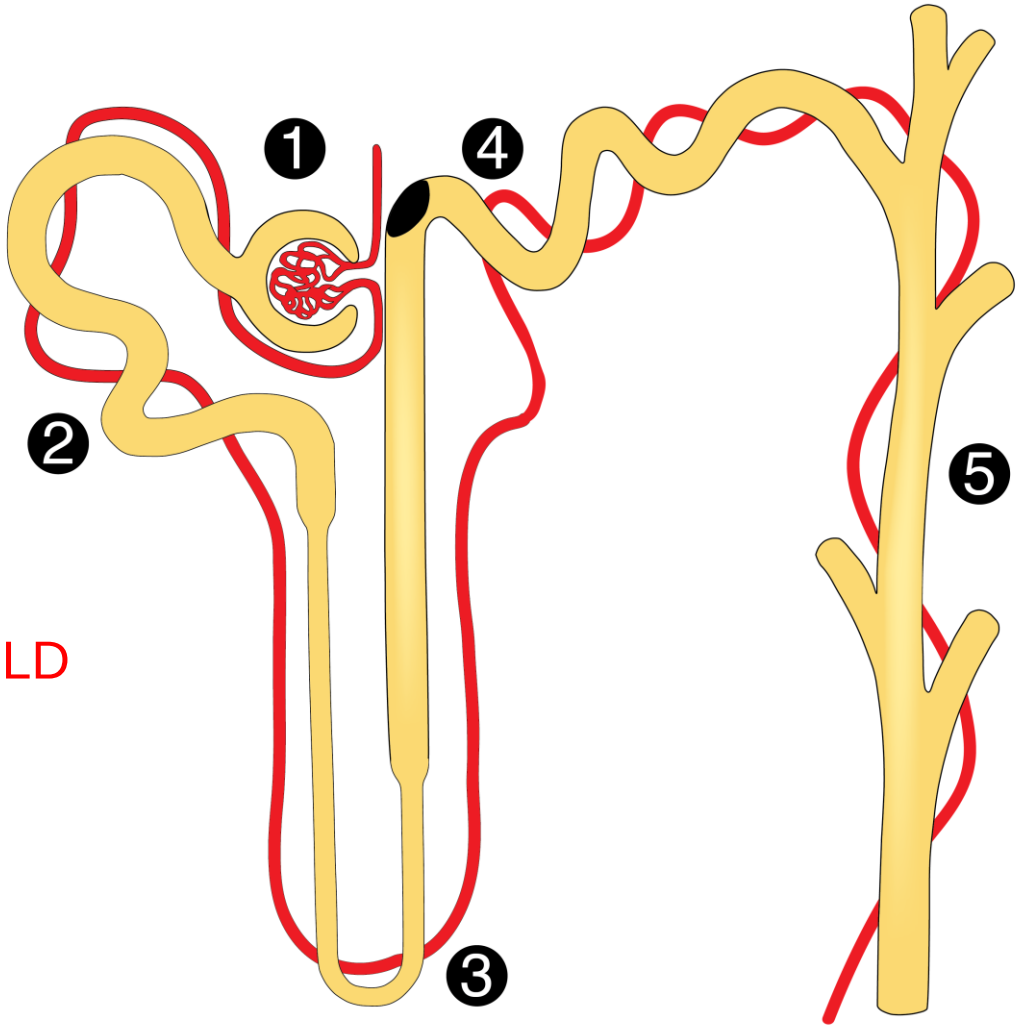
IV: Distal Nephron



Mullens W et al. Eur Heart J, 2017;38:1872-1882

Renal sodium reabsorption occurs mostly in proximal tubules (and is increased in HF)

1. Glomerulus
2. Proximal tubules (60-70%) ⇑ in HF with congestion
3. Loop of Henle (25%)
4. Macula densa
5. Distal / collecting tubules (5%) ⇑ in chronic high-dose LD



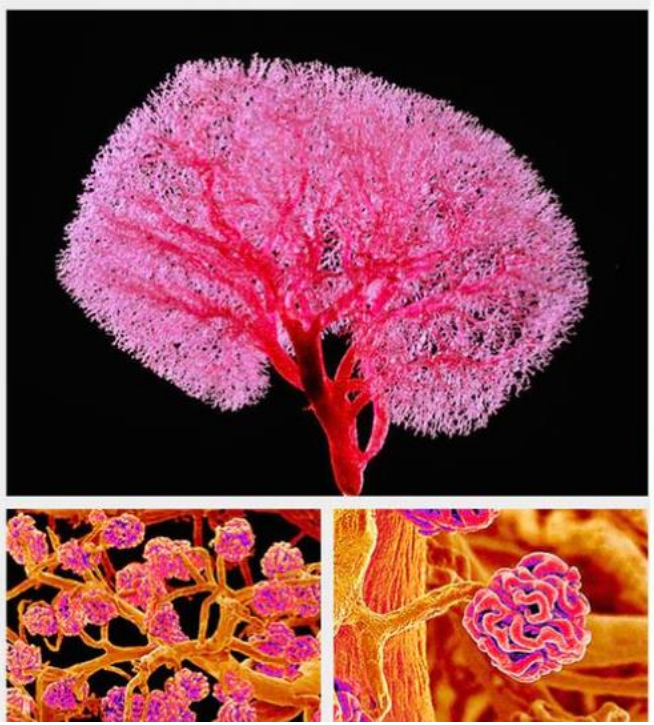
Mullens W et al. Eur Heart J, 2017;38:1872-1882

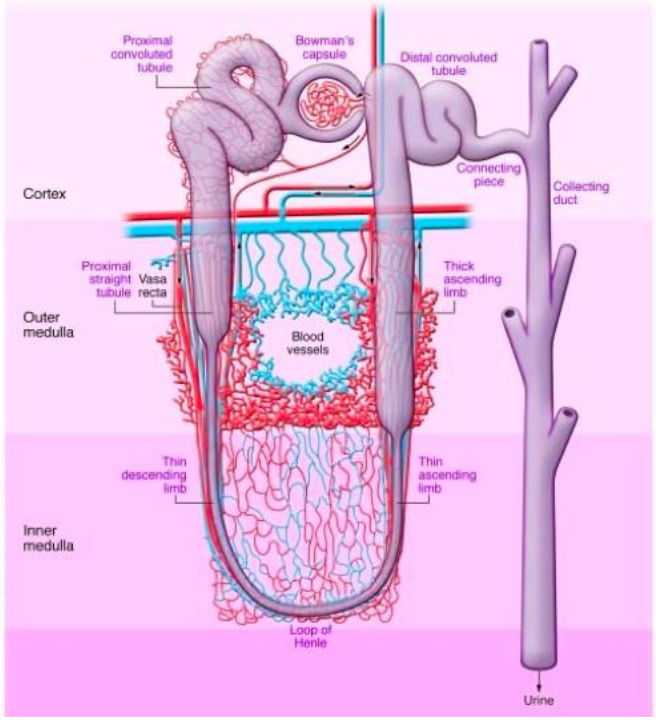
Underappreciated risk for hospitalization / death associated with residual congestion in HF

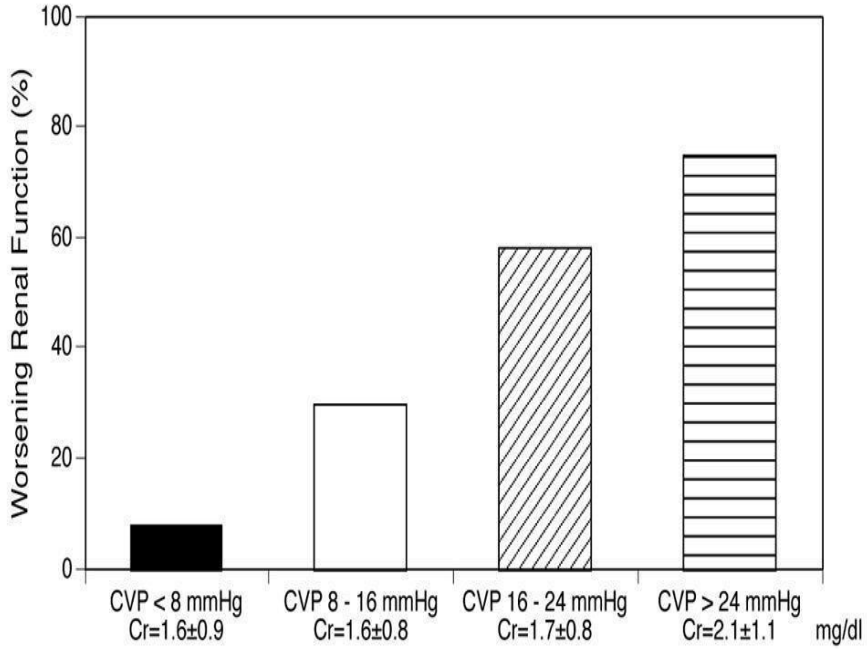
Recommendations	Class[a]	Level[b]
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment.[427,472]	I	C

McDonagh T et al. Eur Heart J 2021

Kidney: a remarkable vascular organ susceptible to congestion







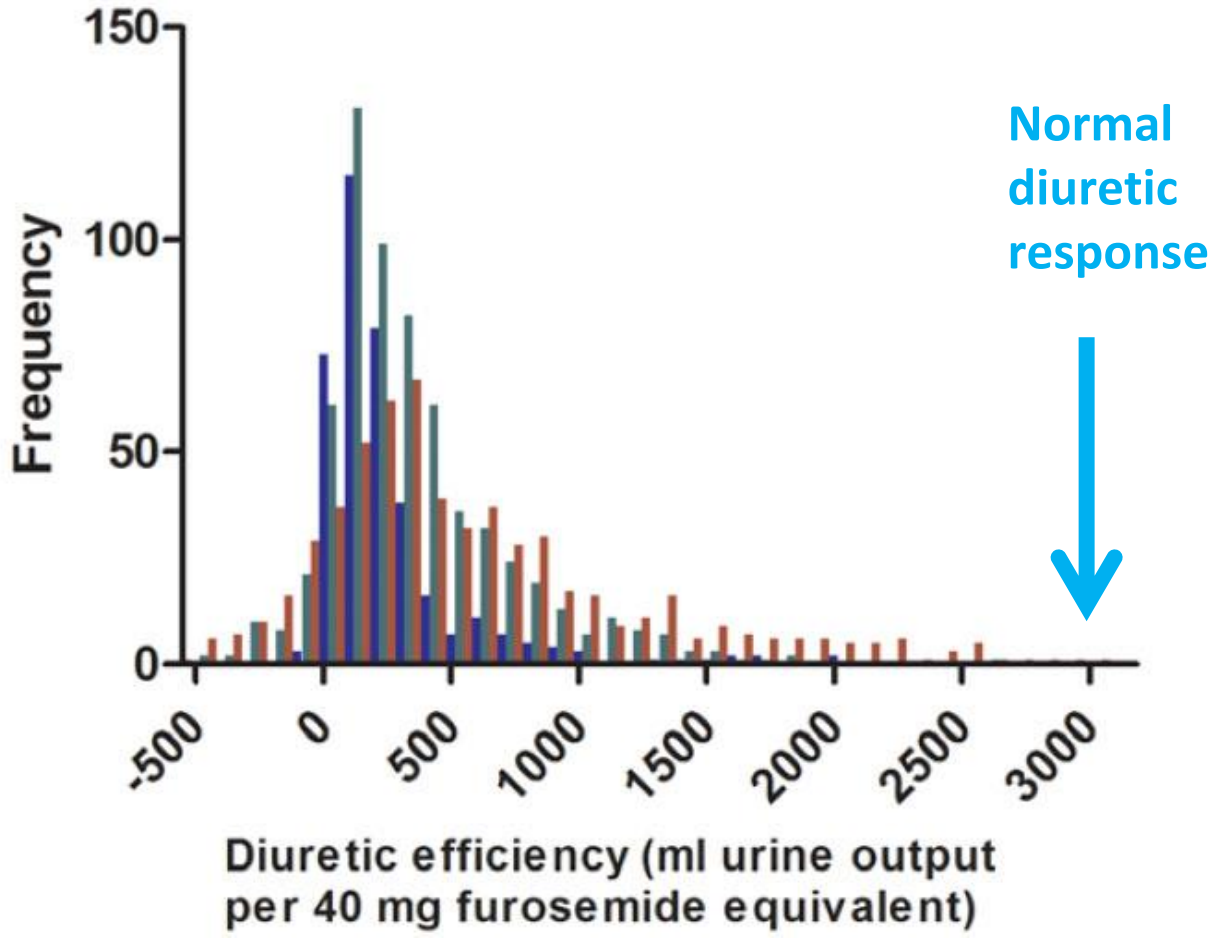
Renal Plasma flow = 600 ml /min
Renal blood flow = 1000 ml/min

Bonventre LI. J Clin Invest 2011
Mullens W et al. J Am Coll Card 2009;53:589-96.

Diuretics		
Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms.[145]	I	C
Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses.[145]	IIa	B

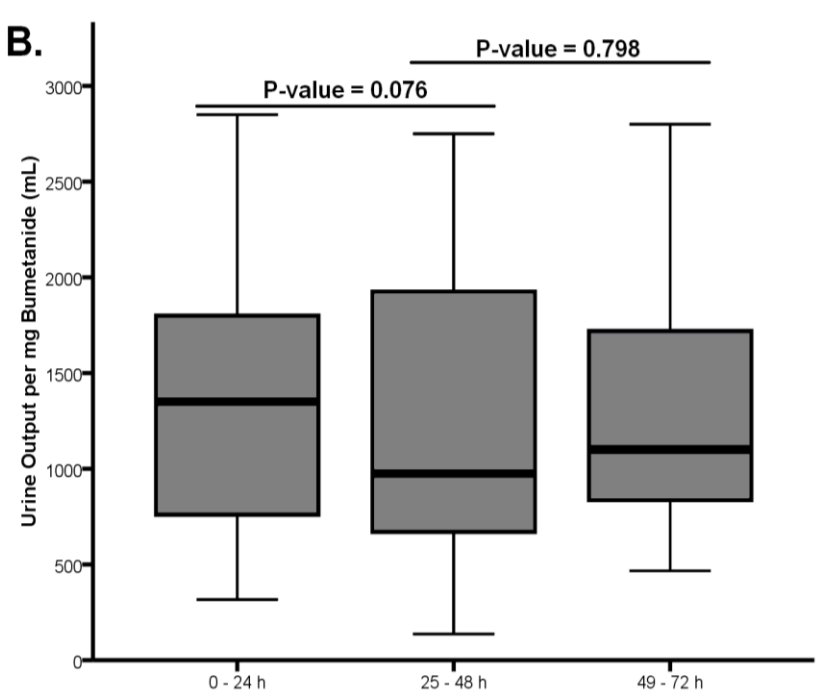
McDonagh T et al. Eur Heart J 2021

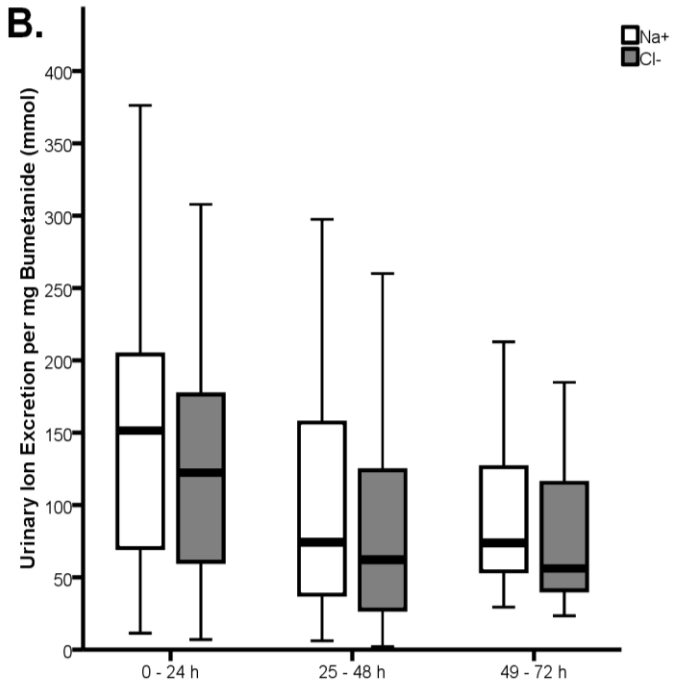
’Diuretic resistance’ is omnipresent in HF patients



Testani J et al. Circ Heart Fail 2014.

Urinary Composition during Decongestion





Progressive decrease in Urinary Na and Cl but NOT in urine output

(even after correction for diuretic dose)

Verbrugge F, Mullens W, et al. Circ Heart Fail 2014.

ESC European Society of Cardiology

European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1369

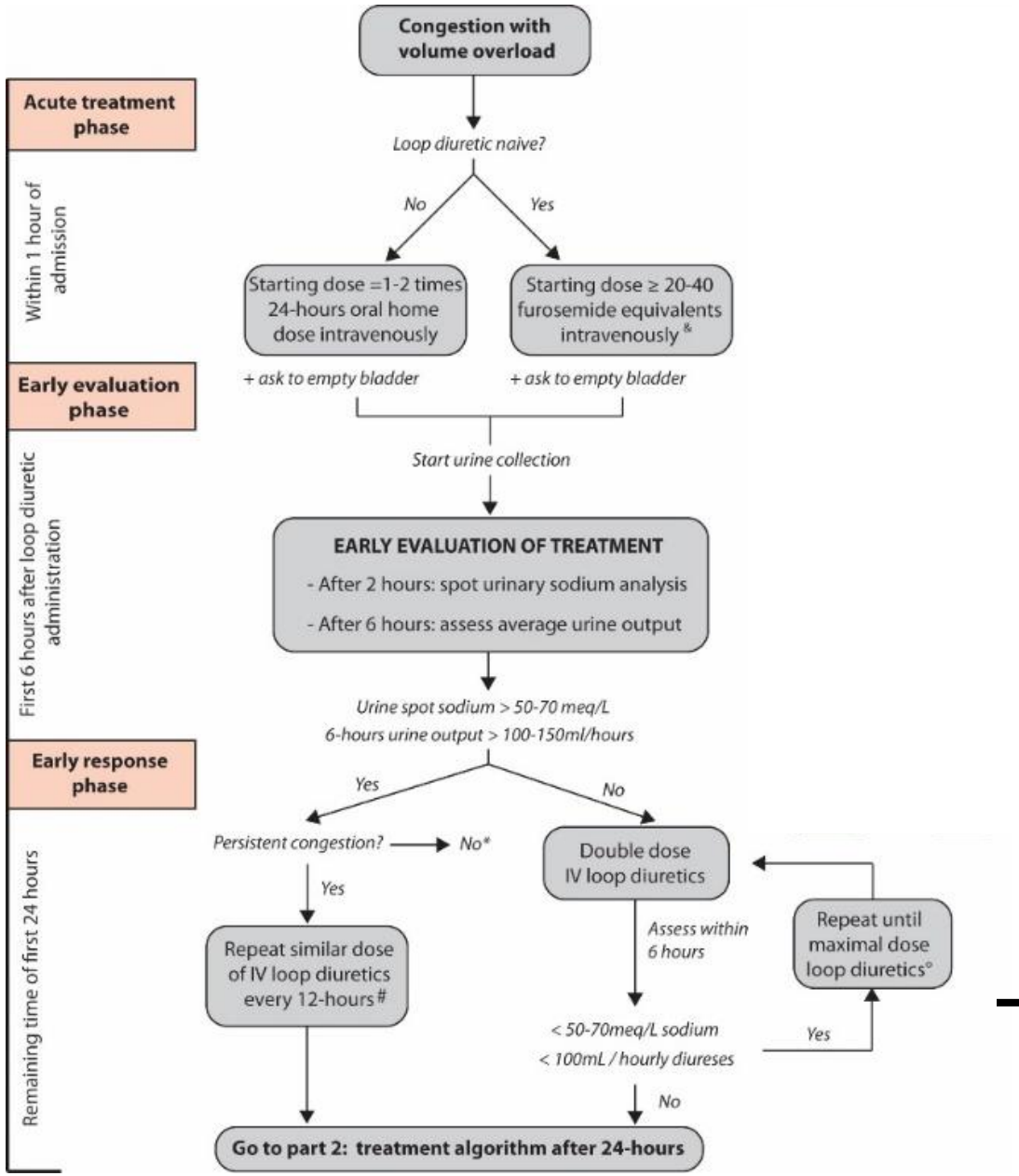
POSITION PAPER

The use of diuretics in heart failure with congestion — a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1,2]*, Kevin Damman[3], Veli-Pekka Harjola[4], Alexandre Mebazaa[5], Hans-Peter Brunner-La Rocca[6], Pieter Martens[1,2], Jeffrey M. Testani[7], W.H. Wilson Tang[8], Francesco Orso[9], Patrick Rossignol[10], Marco Metra[11], Gerasimos Filippatos[12,13], Petar M. Seferovic[14], Frank Ruschitzka[15], and Andrew J. Coats[16]

Citations: > 600
Downloads: > 500.000

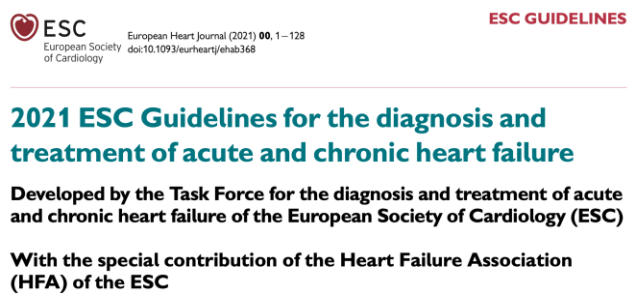
Mullens W, Eur J Heart Fail 2019; 21:137-155.



Five most important rules

1) Door to diuretic time
2) Early evaluation (within HOURS) of the diuretic effect
3) Appropriate dosing according to natriuresis/diuresis
4) Only stop when the patient is ‘dry’
5) Continue guideline-directed medical therapy

Incorporated



(590 citations)

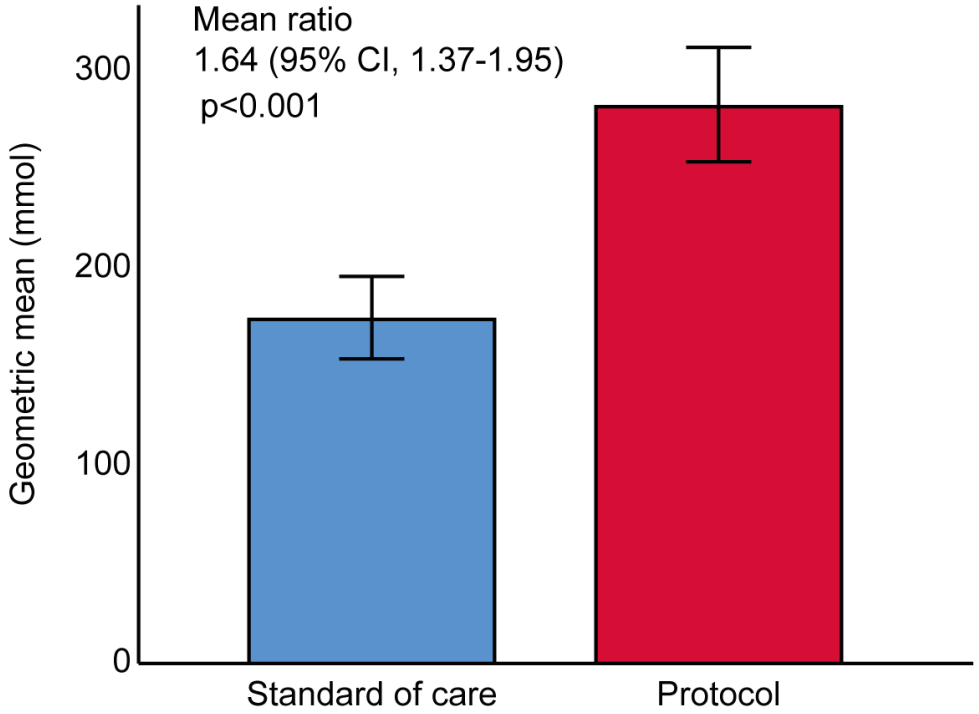
Mullens W, Eur J Heart Fail 2019; 21:137-155.

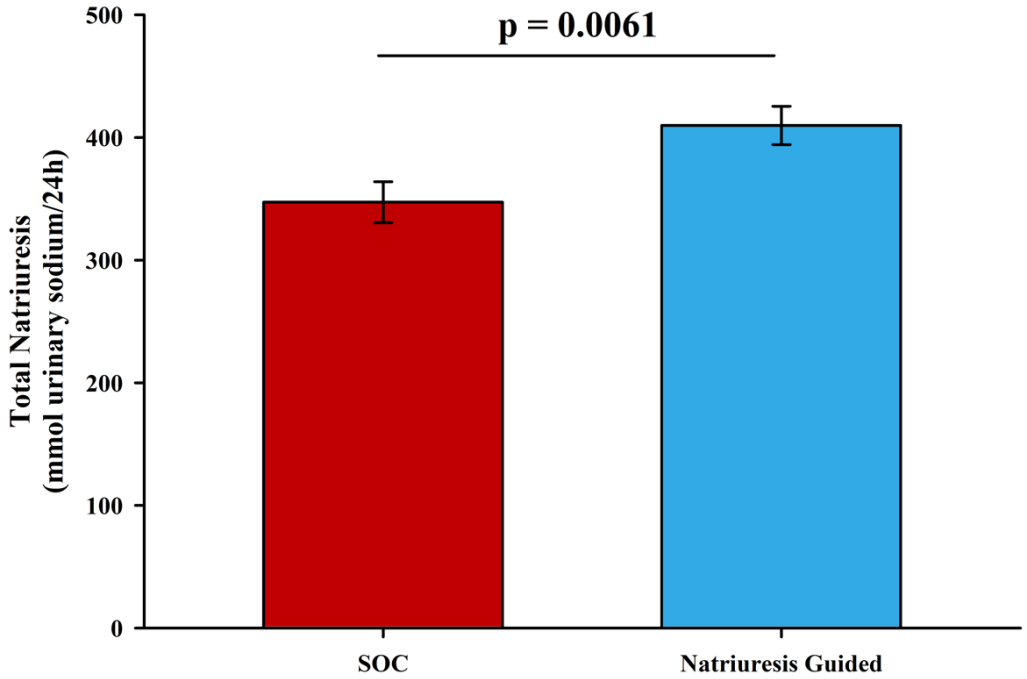
Desalination RCTs

ENACT-HF Study

PUSH-AHF trial

Primary endpoint: natriuresis after 24 hours

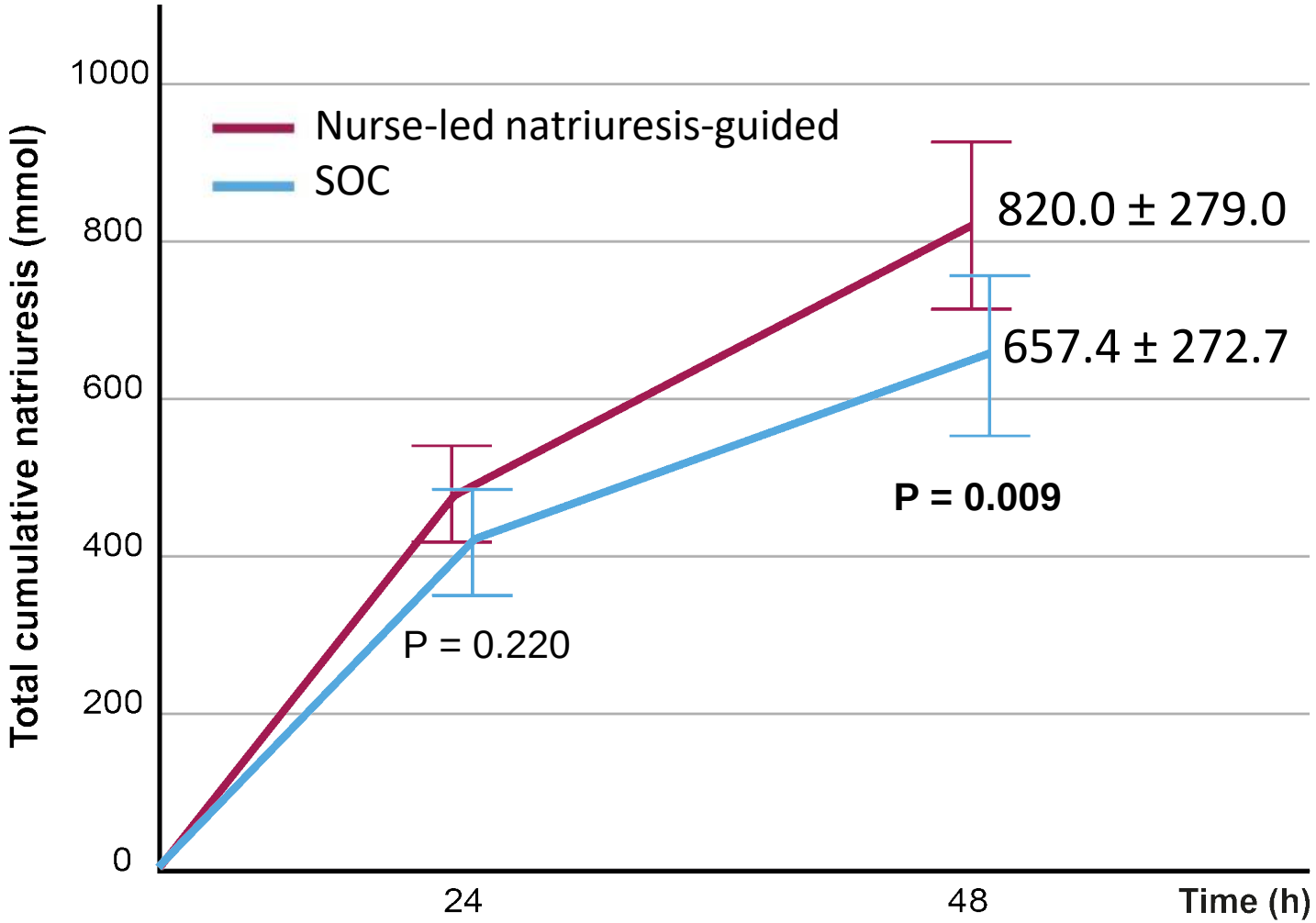




Ongoing:
DECONGEST (NCT05411991)
ESCALATE (NCT04481919)

Dauw J, Mullens W et al. Circ Heart Fail, in press 2024
Ter Maaten J et al. Nat Med 2023;29:2625-2632

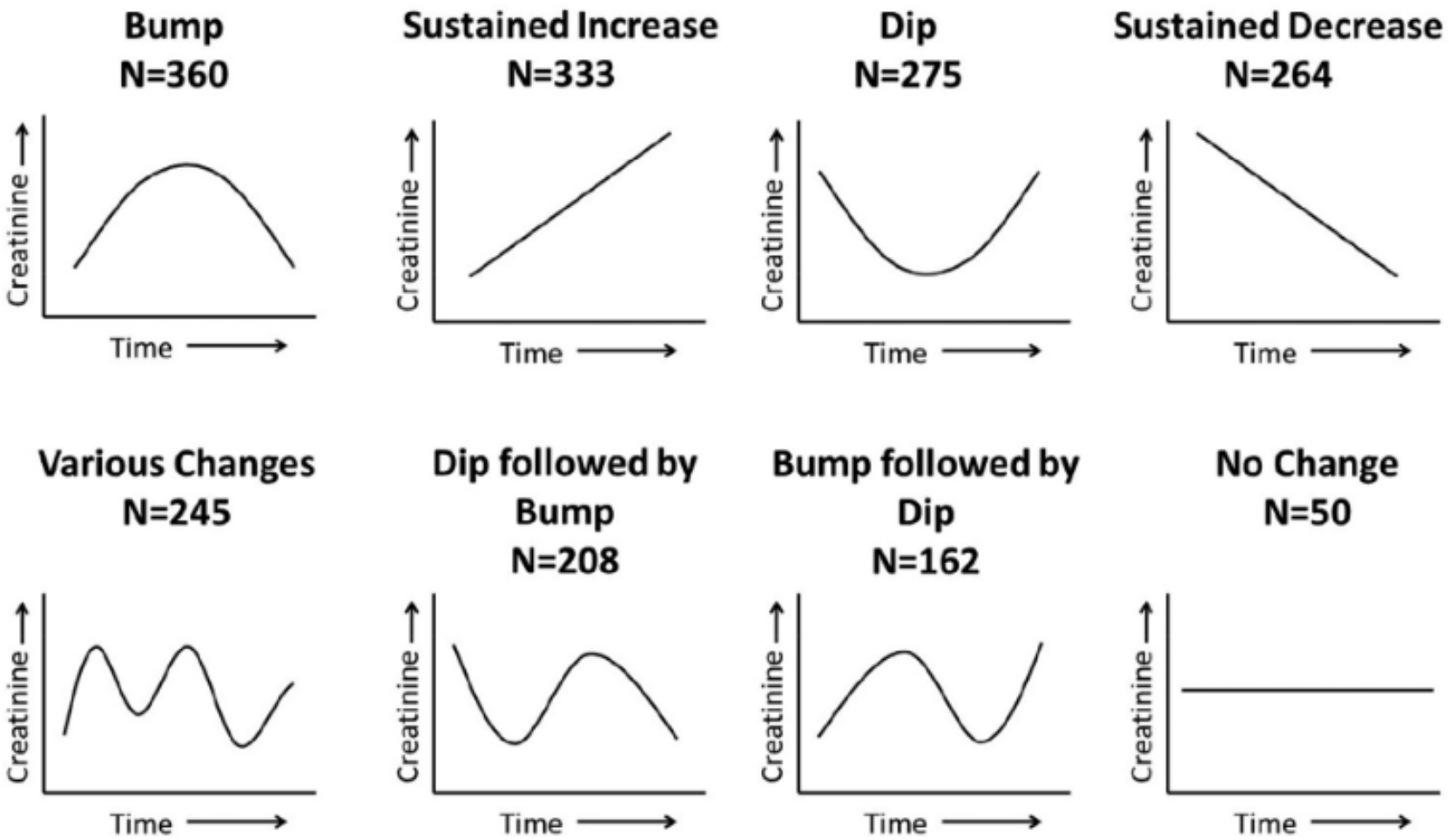
Nurse-Led Diuretic Titration via POC Urinary Sodium Sensor in ADHF
EASY-HF trial



P = 0.027
Absolute difference
163 (19 to 306)

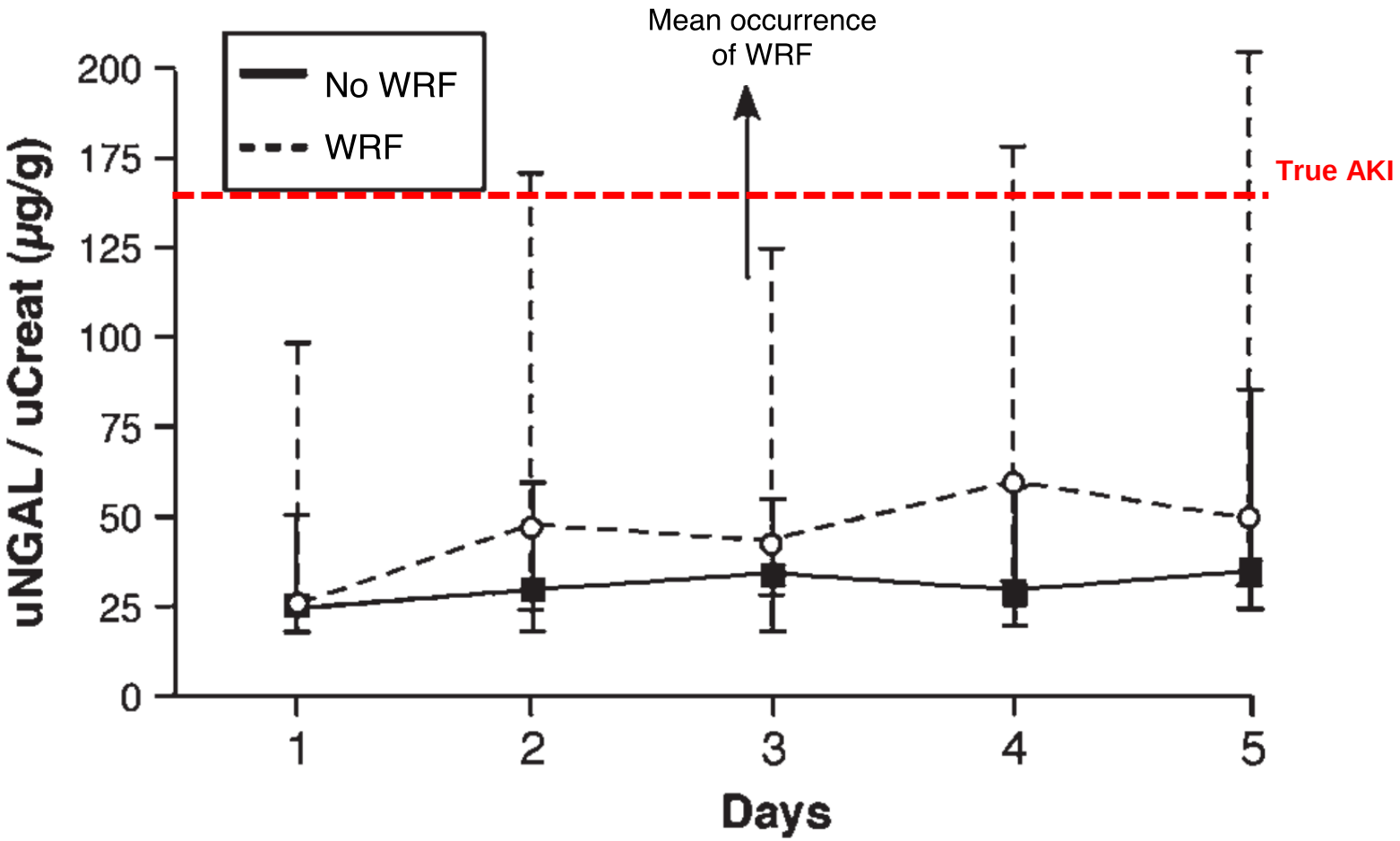
Meekers E, Mullens W. Eur J Heart Fail. 2024 In press.

Worsening renal function during Acute HF



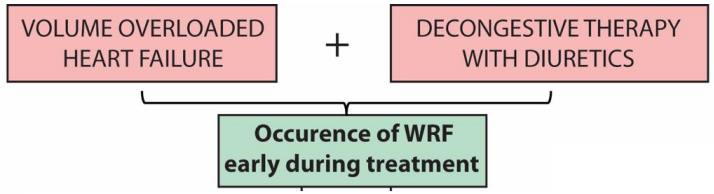
Beldhuis E, Damman K et al. J Card Fail 2019;25:866-874.

WRF during AHF does NOT lead to permanent renal damage



Dupont M. Eur J Heart Fail 2012;14:597-604.

Worsening renal function during Acute HF



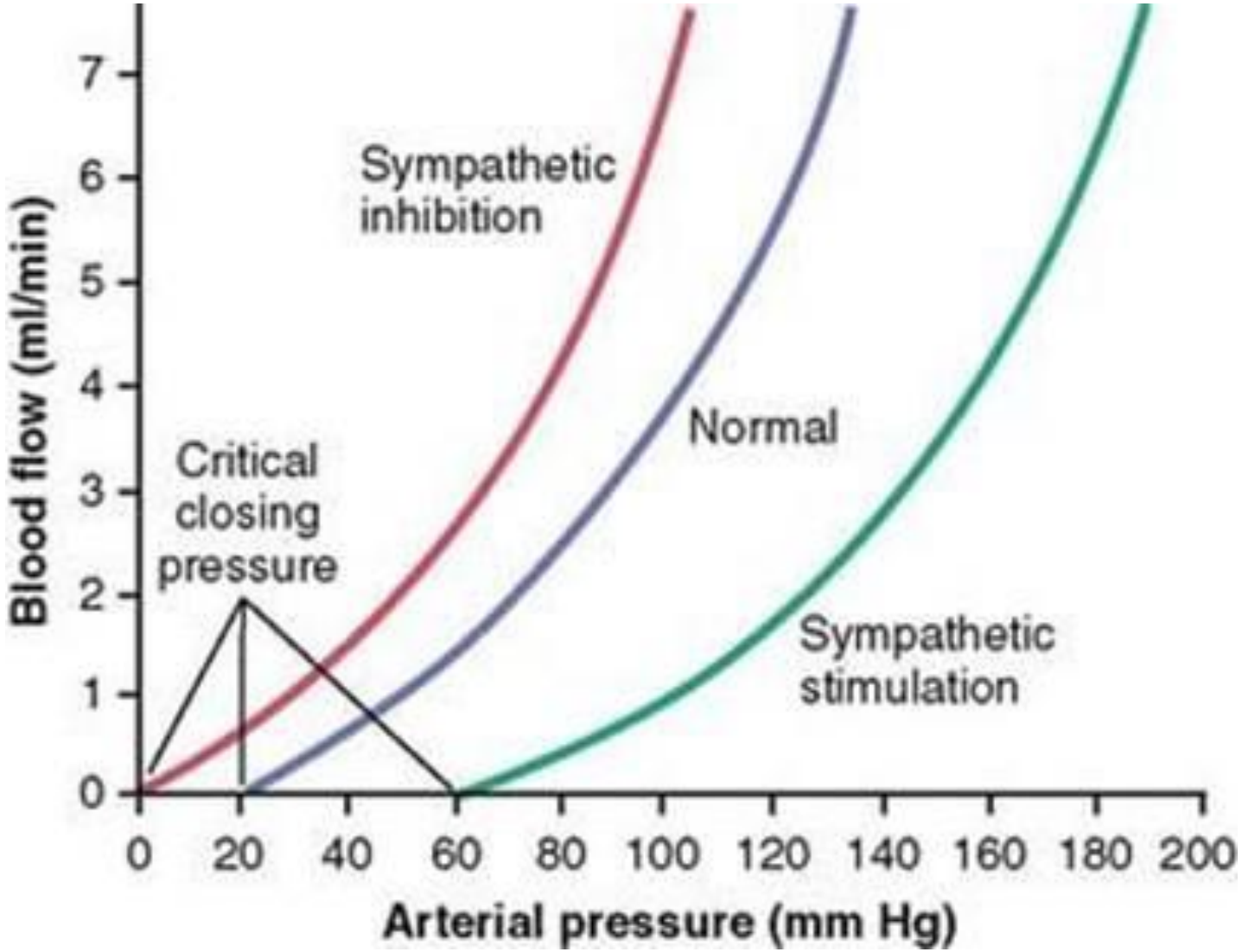
CAUTION IN CASE OF

- *Serum creatinine increases more than 100%*
- *Serum creatinine absolute increase above 3.5 mg/dl*

99% 1%

Mullens W, Eur J Heart Fail 2020; 22:584-603.

Pathophysiology: blood pressure ≠ flow



Guyton and Hall Textbook of Medical Physiology, Chapter 14

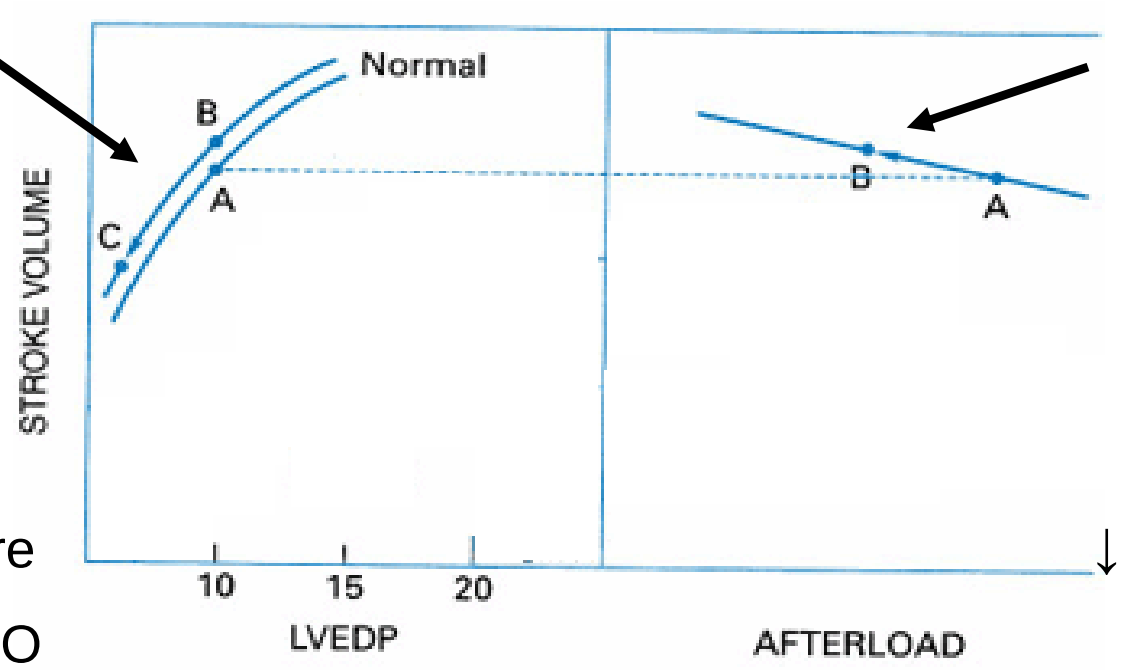
Pathophysiology: pre- and afterload normal heart

Vasodilator

↓ Stroke Vol

↓ Blood pressure

BP = SVR x CO



Vasodilator

↓ SVR

↓ Blood pressure

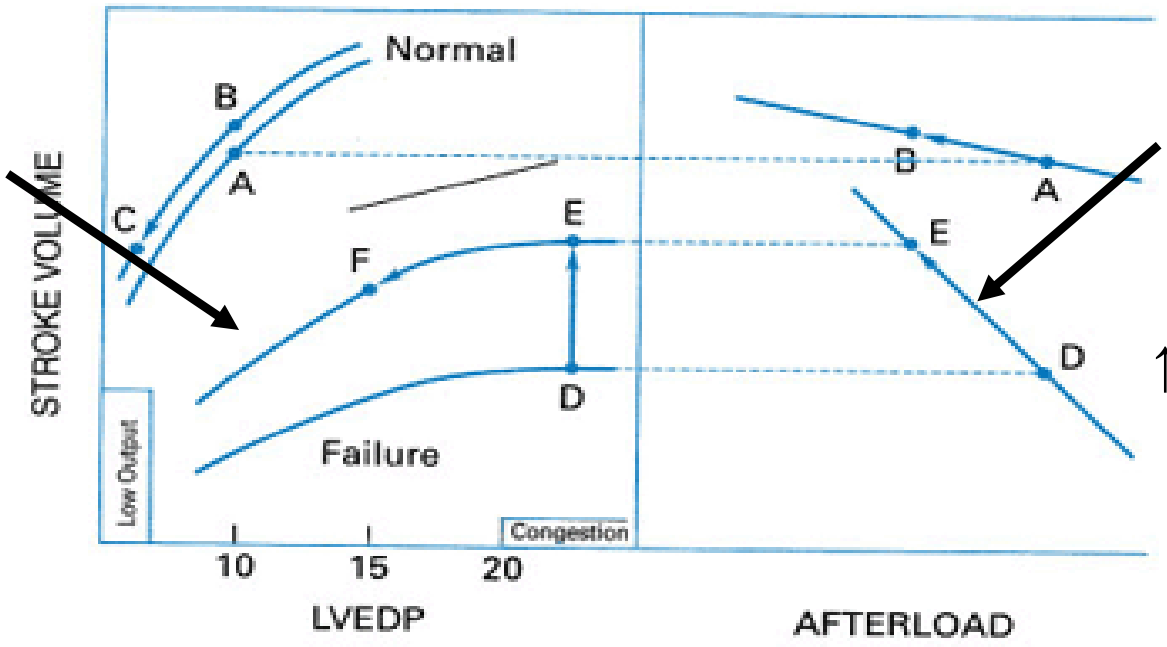
BP = SVR x CO

Normal heart = “preload” dependent

Pathophysiology: pre- and afterload failing HFrEF

Vasodilator

↑ Stroke Vol



Vasodilator

↑ Stroke vol

Stroke volume = preload – afterload

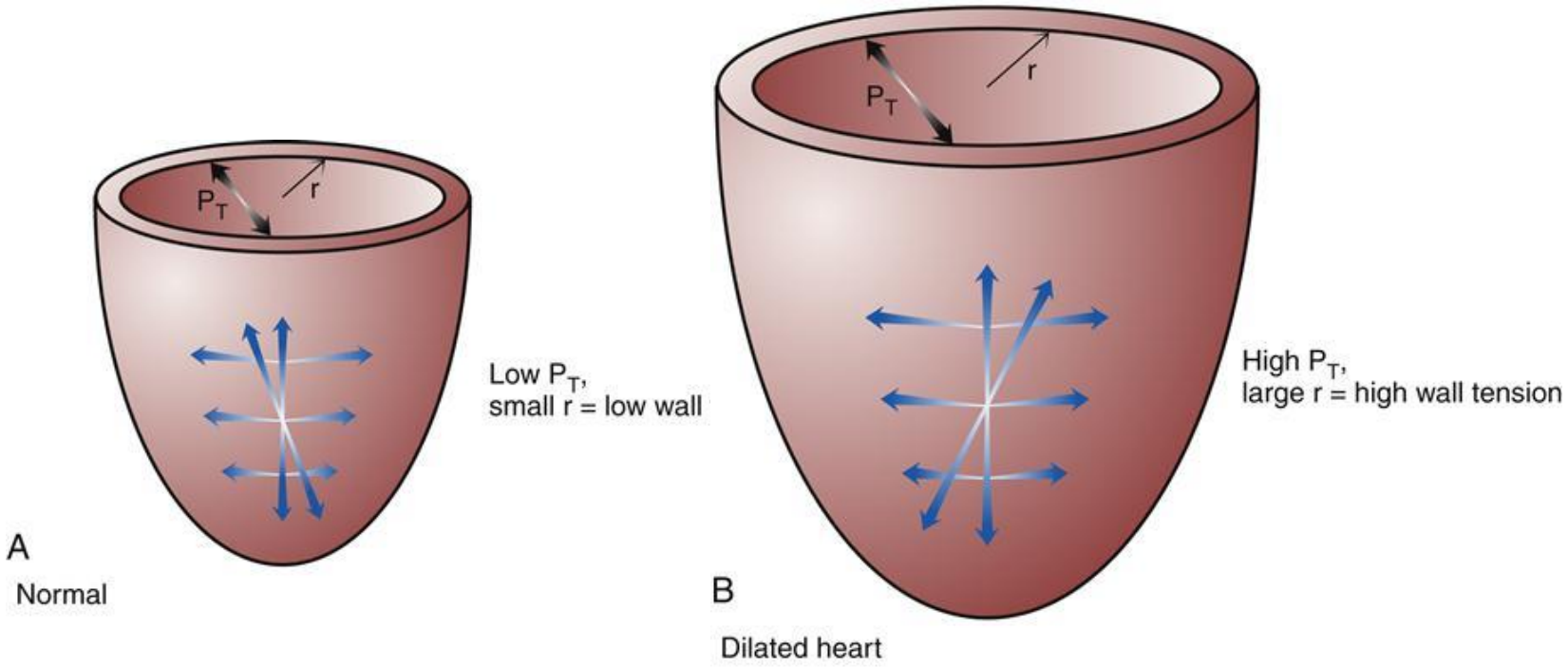
Normal heart = “preload dependent”

Heart failure = “afterload dependent”

SVR ↓, CO ↑ (BP = “afterload”)

What is LV afterload ?

Pathophysiology: failing HFrEF – Law of Laplace



Wall tension = (pressure x radius) / (2x wall thickness)

Pathophysiology: failing HFrEF
Nitroprusside for Advanced Decompensated HFrEF

Start **Nitroprusside** protocol through a continuous infusion at a dose of 10-400 mcg/min (without bolus)

Titrate to MAP 60-70 mmHg

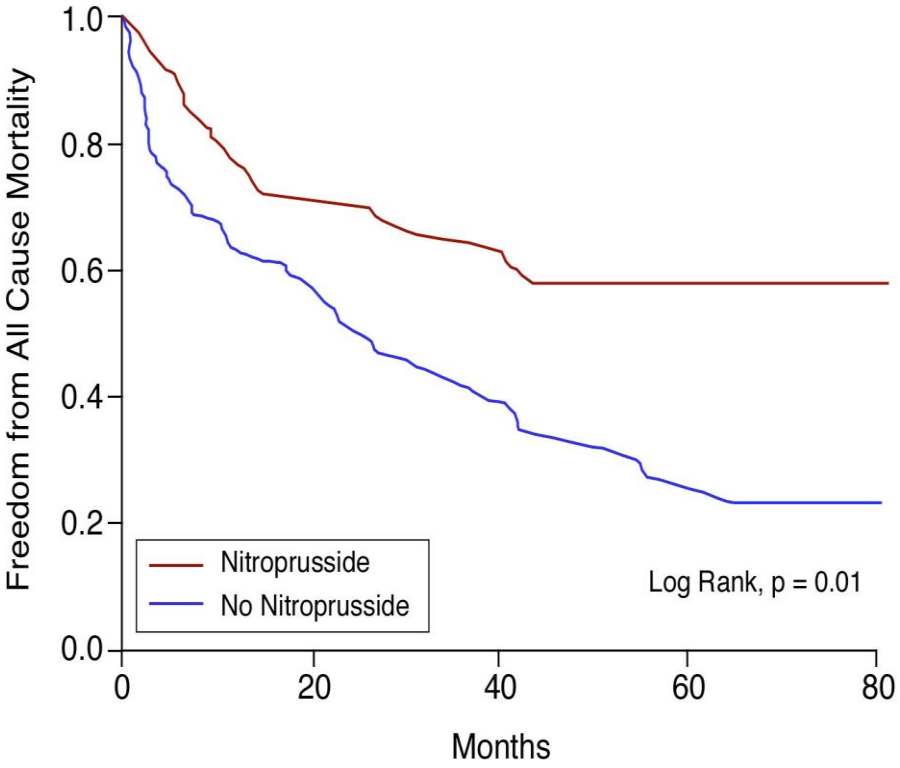
Well trained nursing staff – dose adjusted / 15 minutes

BP measured non-invasively

Optimal hemodynamic response

- decrease in PCWP to ≤ 18 mmHg,
- decrease in right atrial pressure to ≤ 8 mmHg
- improvement in cardiac index to ≥2.2 l/min/m2

Continue ACE-I, BB and spironolactone as tolerated



Mullens W et al. J Am Coll Card 2008;52:200-7.

High dose spiro for advanced decompensated heart failure
ATHENA trial

	Usual Care	Spironolactone	P
Log NTproBNP			
Baseline	8.23 (7.58, 8.94)	8.43 (7.90, 9.17)	
96 h (or discharge)	7.64 (6.93, 8.45)	7.89 (7.19, 8.68)	
Change	-0.49 (-0.98, -0.14)	-0.55 (-0.92, -0.18)	0.57
N-terminal pro B-type natriuretic peptide, pg/ml			
Baseline	3753 (1968, 7633)	4601 (2697, 9596)	
96 h (or discharge)	2080 (1025, 4675)	2672 (1326, 5896)	
Change	-1072 (-3182, -231)	-1796 (-3883, -571)	0.76

Butler J et al. JAMA Cardiol. 2017;2:950-958

Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses.[145]	IIa	B

McDonagh T et al. Eur Heart J 2021

CLOROTIC

Endpoint	Placebo ($n = 116$)	Hydrochlorothiazide ($n = 114$)	*P*-value
Coprimary endpoints			
Change in weight at 72 h (kg)	−1.5 (−3.2 to 0.0)	−2.3 (−3.9 to −1.2)	0.002
Adjusted estimated difference (notionally 95% confidence interval)	−1.14 [−1.84 to −0.42]		
AUC for dyspnoea at 72 h (VAS)	720 (240–1455)	960 (360–1620)	0.497

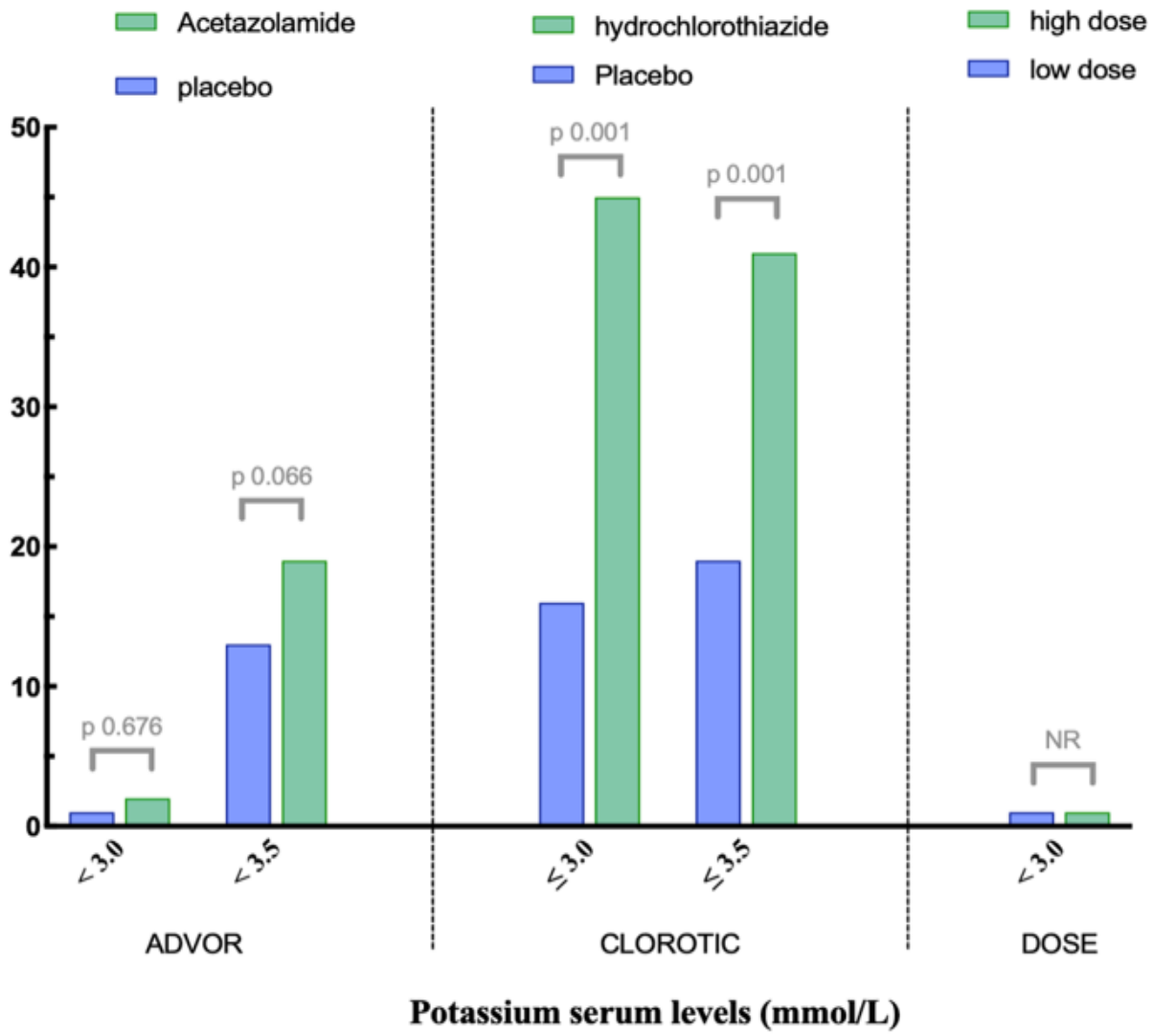
Trullas JC et al. Eur Heart J 2023;44:411-421

Subanalysis CLOROTIC trial: less effect if eGFR was lower !

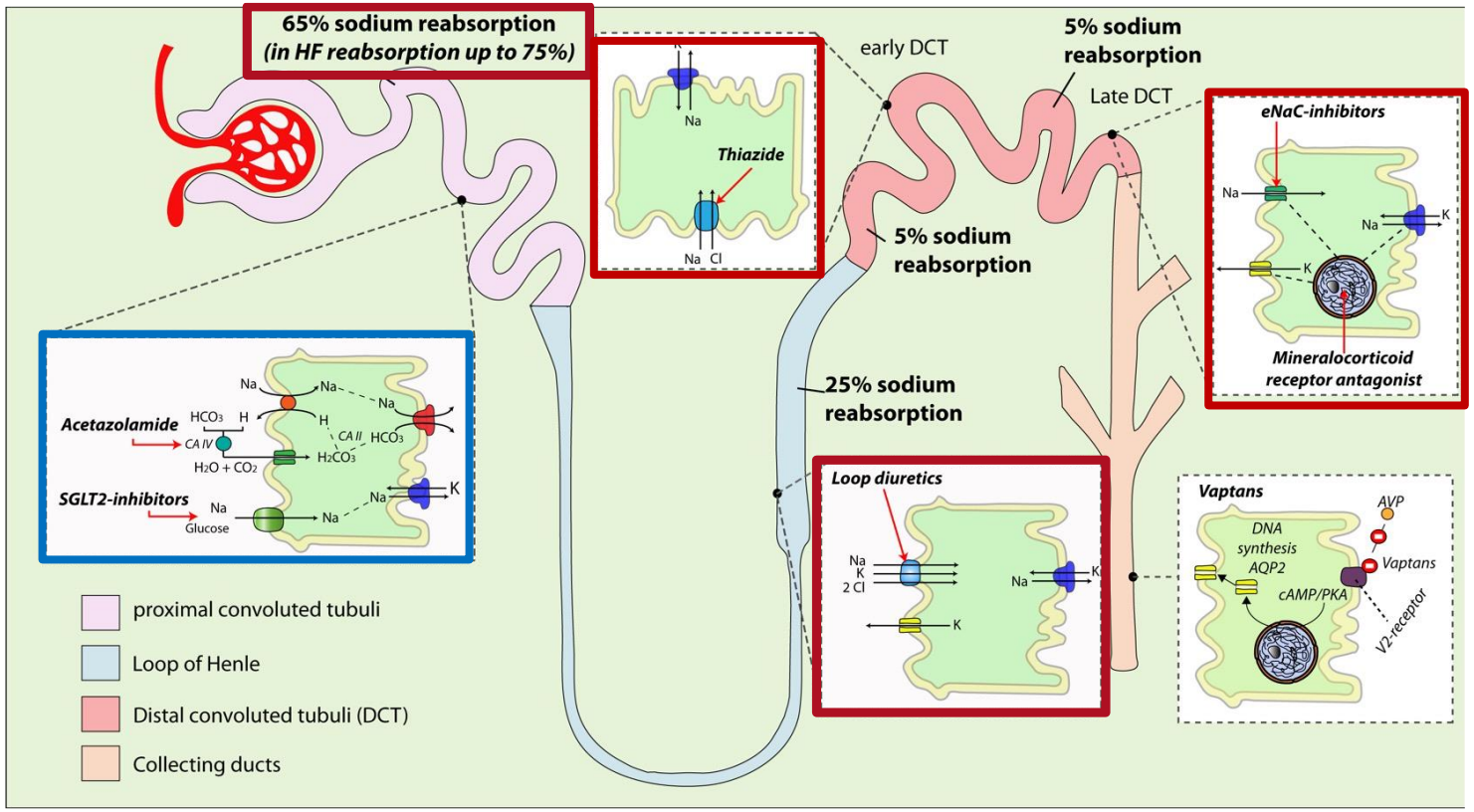
	Results for placebo	Results for HCTZ	Difference	P for interaction
Primary endpoint. Change in weight (kg) at 72 hours				
Overall	-1.6 [-2.1 to 1.1]	-2.4 [-2.7 to -1.8]	-0.8 [-1.4 to -0.2]	**0.001**
< 45 ml/min/1.73m^2	-1.8 [-2.3 to -0.9]	-1.9 [-2.4 to -1.7]	-0.1 [-1.3 to 0.4]	0.246
45 to 59 ml/min/1.73m^2	-1.2 [-2.1 to -0.7]	-2.5 [-3.3 to -0.9]	-1.3 [-2.3 to 0.2]	
≥ 60 ml/min/1.73m^2	-1.6 [-2.9 to -1.2]	-3.7 [-4.8 to -2.7]	-2.1 [-3.0 to -0.5]	

Trullas JC et al. Eur J Heart Fail 2023;25:1784-1793

Hypokalemia loop diuretics +/- acetazolamide vs thiazides



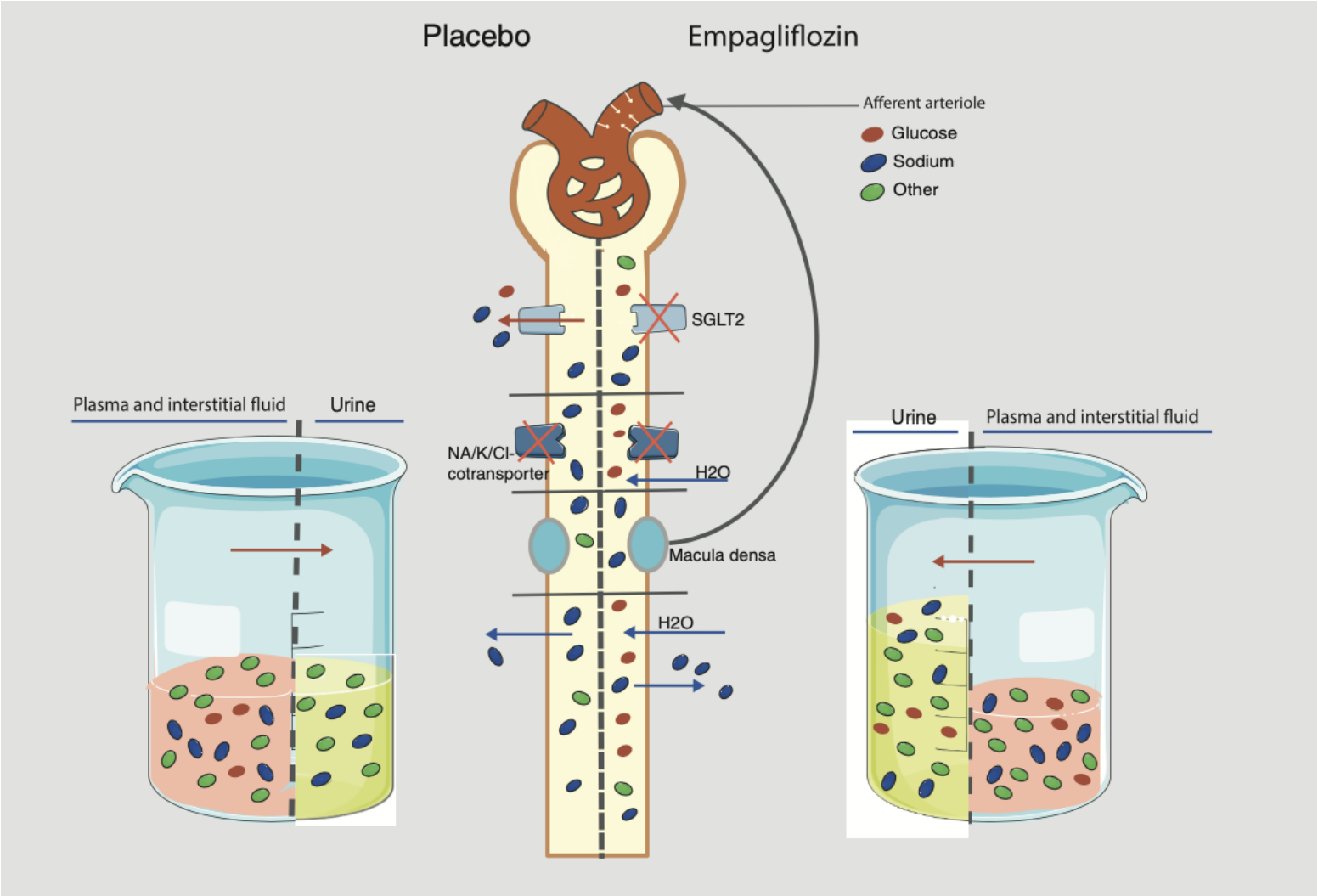
D'Hondt S, Mullens W et al. Eur J Heart Fail 2023; 25:1310-1319



HF induces a state of increased proximal renal sodium reabsorption, but loop diuretics, thiazides, MRA work distal at loop of Henle

Mullens W et al. J Am Coll Card 2009;53:589-96.
Mullens W et al. Eur J Heart Fail 2019; 21:137-155

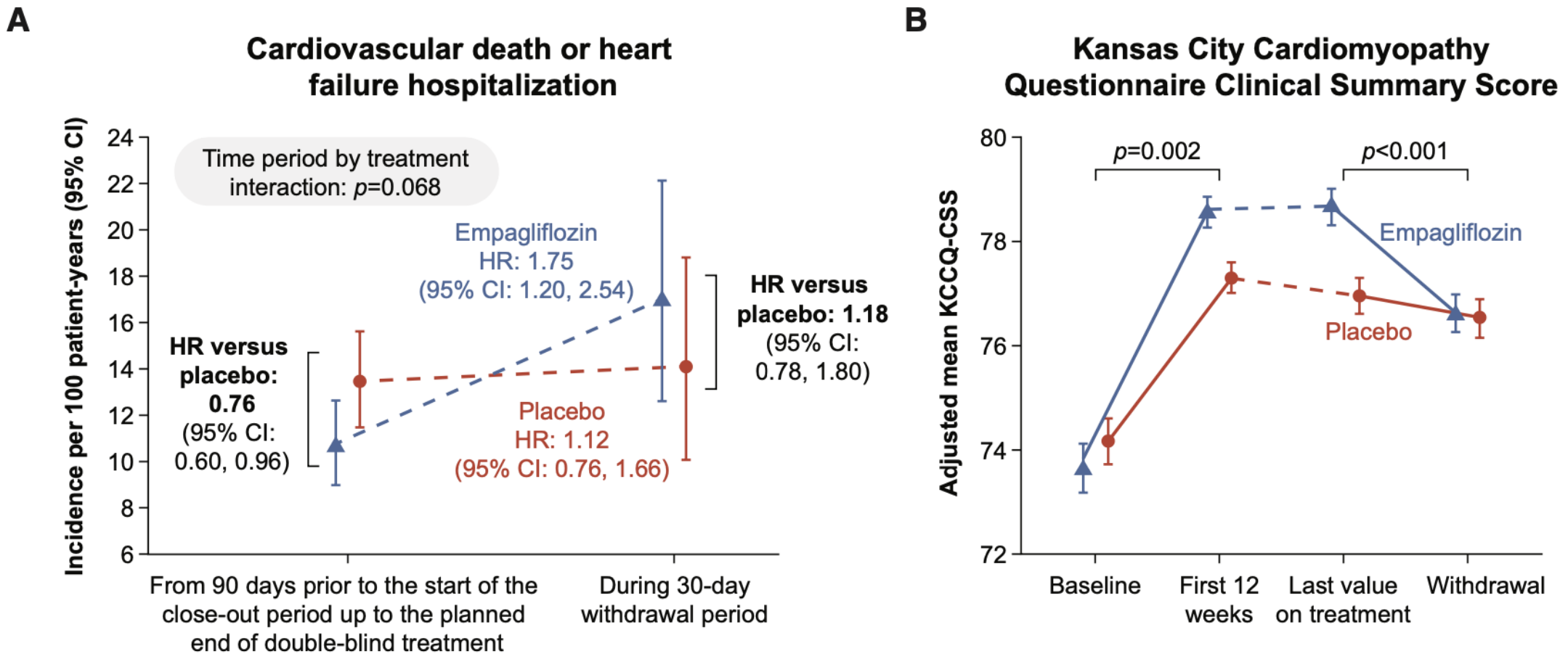
Renal Preservation: SGLT2i (EMPA-RESPONSE-AHF)



↑ FeGluc but = FeNa

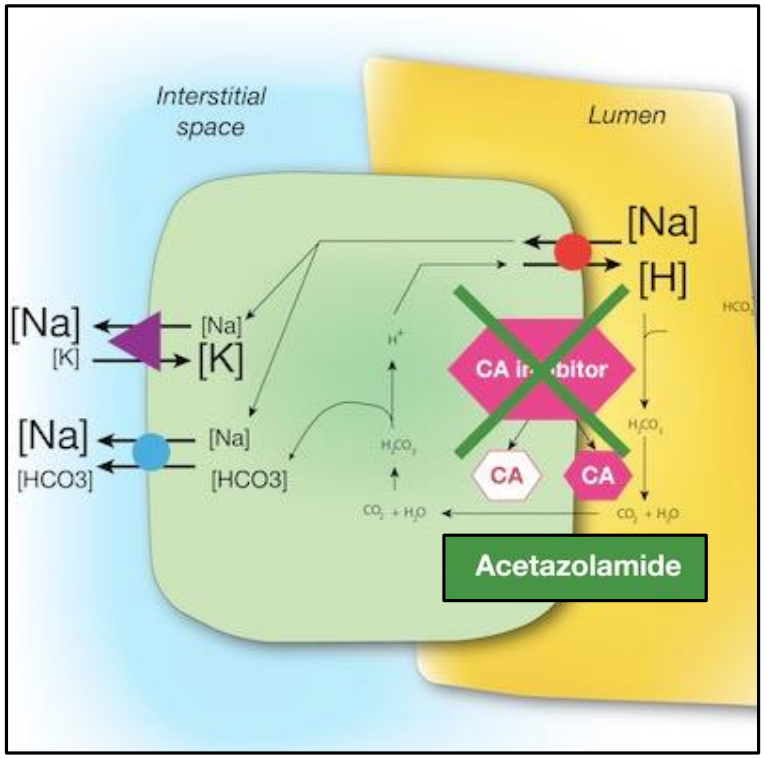
Boorsma E et al. Eur J Heart Fail, 2021;23:68-78

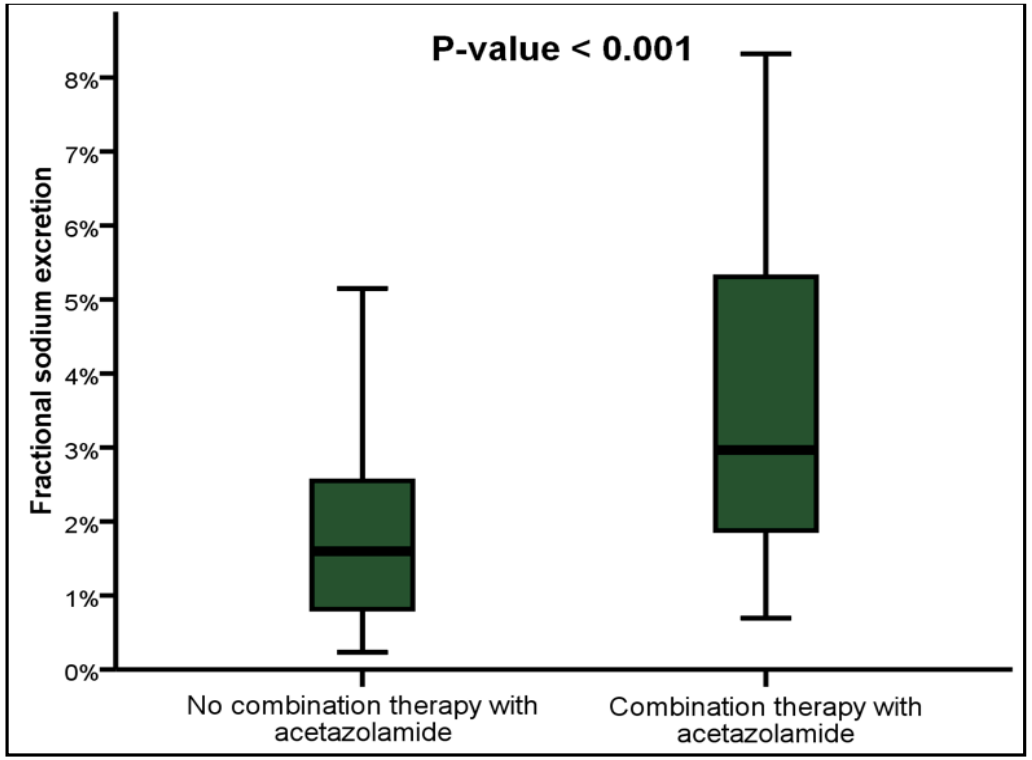
Safe to stop SGLT2i ?



Packer M et al.Circulation 2023

Acetazolamide might improve loop diuretic efficiency





Mullens W et al. Eur Heart J 2017
Verbrugge F et al. Acta Cardiol 2015 + Eur J Heart Fail 2019

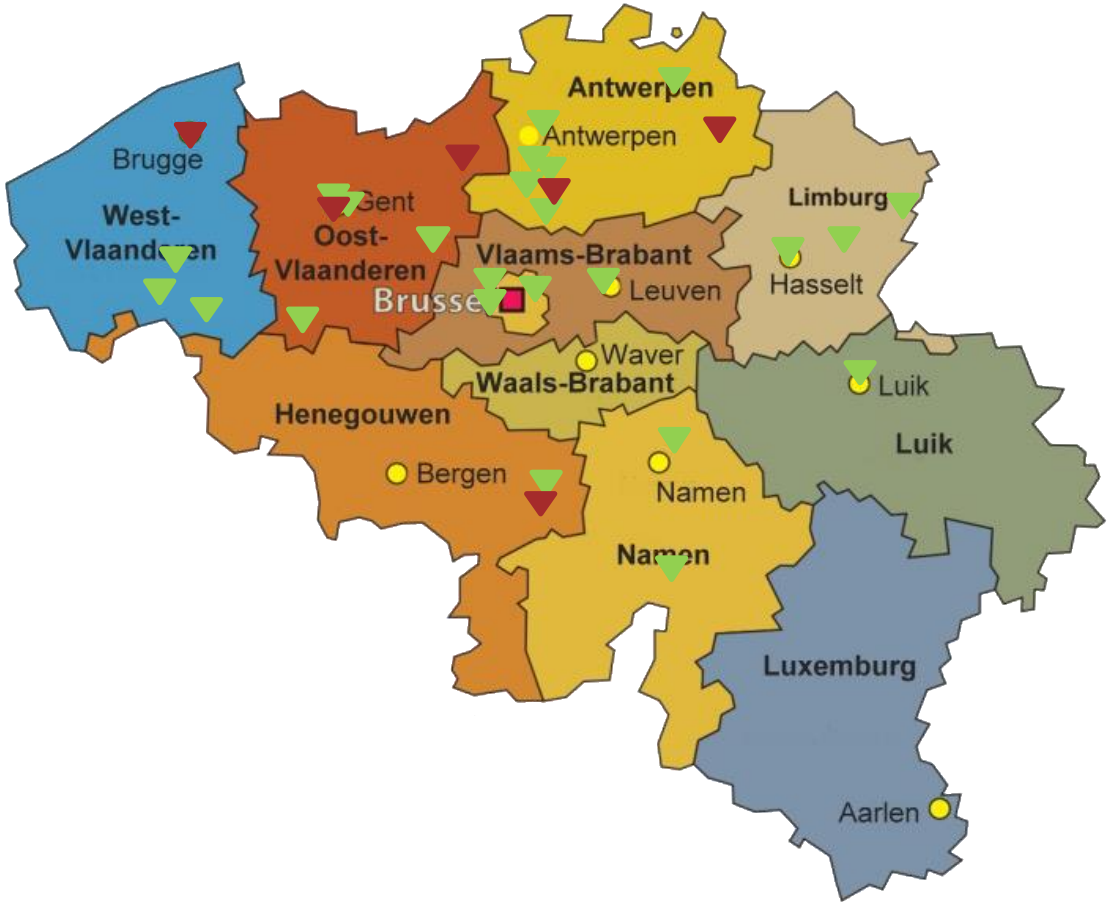
Acetazolamide in **D**ecompensated Heart Failure With **V**olume **O**ve**R**load

www.advor.be

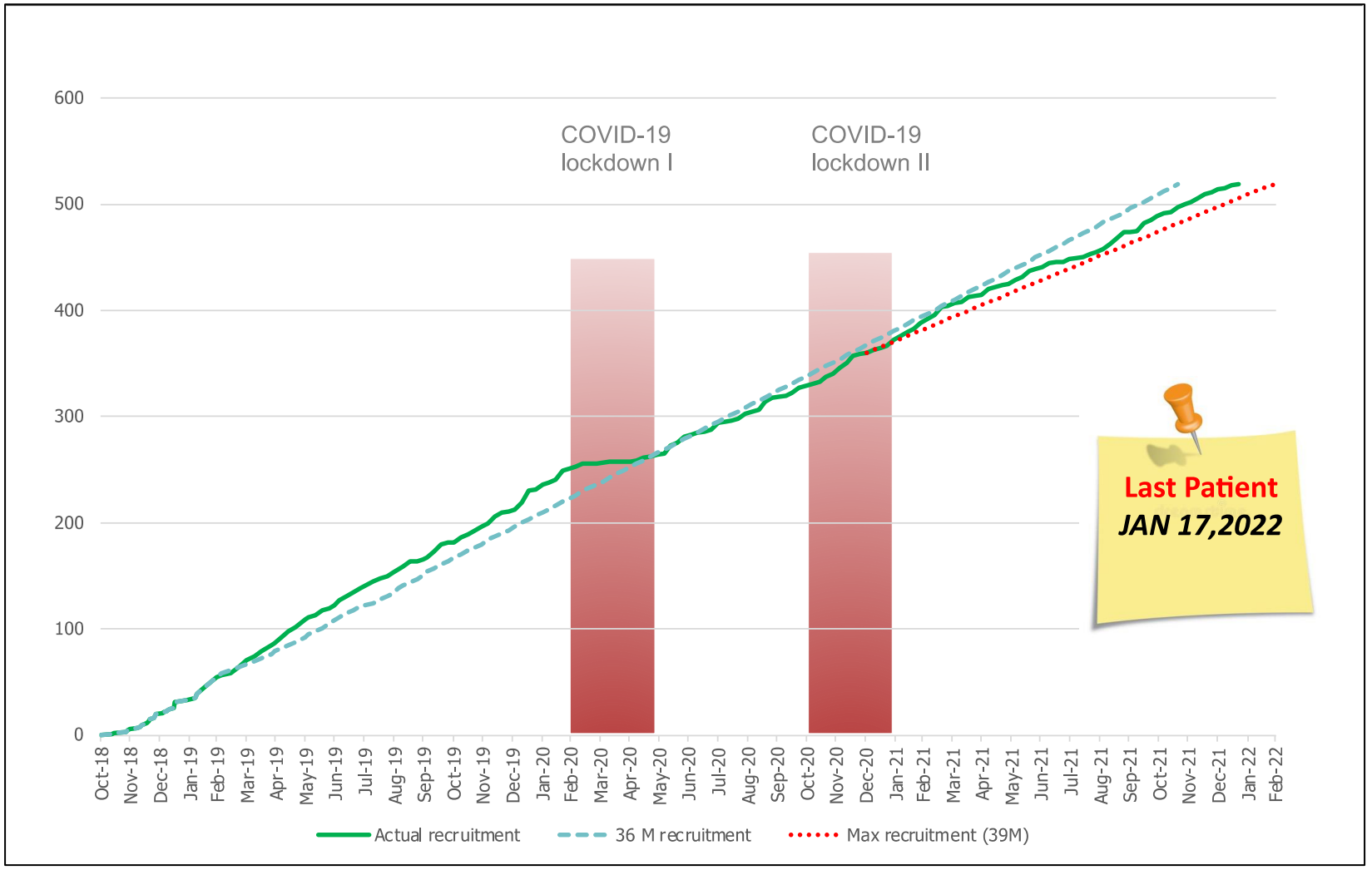
29 (27) participating sites

Hospital	Principal Investigator
AZ Delta Roeselare-Menen	M. Deceunick
AZ Glorieux, Ronse	F. Van Durme
AZ Groeninge, Kortrijk	D. Derthoo
AZ klina, Antwerpen	W. Smolders
AZ Maria Middelares Gent	D. Vervloet
AZ Mol	H. Striekwold
AZ Nikolaas, St-Niklaas	K. Goossens
AZ Sint-Lucas, Gent	H. Vandekerckhove
AZ Turnhout	P.J. Hofkens
CHR de la Citadelle, Luik	P. Troisfontaines
CHU Charleroi	S. Moubayed
CHU UCL Namur	L. Gabriel
Clinique Saint-Luc Bouge	P. Blouard
Grand Hôpital de Charleroi	F. Chenot
GZA, sint-Vincentius, Wilrijk	D. Raes

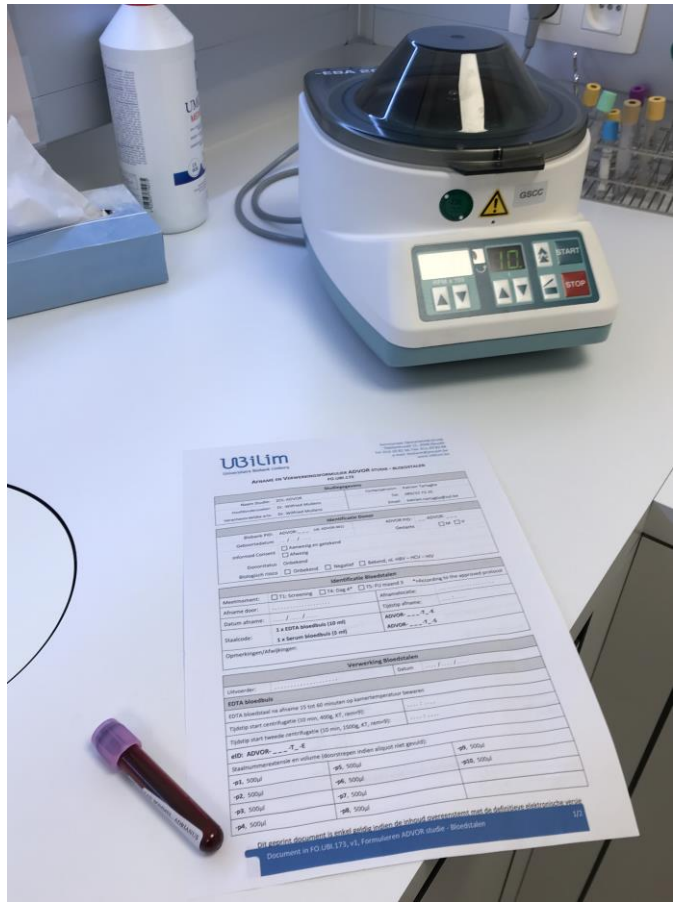
Hospital	Principal Investigator
Hôpital Erasme, Brussel	J.L. Vachiery
Imeldaziekenhuis, Bonheiden	B. Ector
Jan Yperman	E. Viaene
Jessa Ziekenhuis, Hasselt	P. Timmermans
OLV Ziekenhuis Aalst-Asse-Ninove	R. Dierckx
Sint Maarten, Mechelen	G. Vervoort
UZ Antwerpen	E. Van Craenenbroeck
UZ Brussel	S. Lochy
UZ Gent	M. Depauw
UZ Leuven	W. Droogne
UZ Saint-Luc, Brussel	A.C. Pouleur
Ziekenhuis Maas en Kempen	M. Hulselmans
Ziekenhuis Oost Limburg AV	W. Mullens
ZNA Middelheim	E. Prihadi

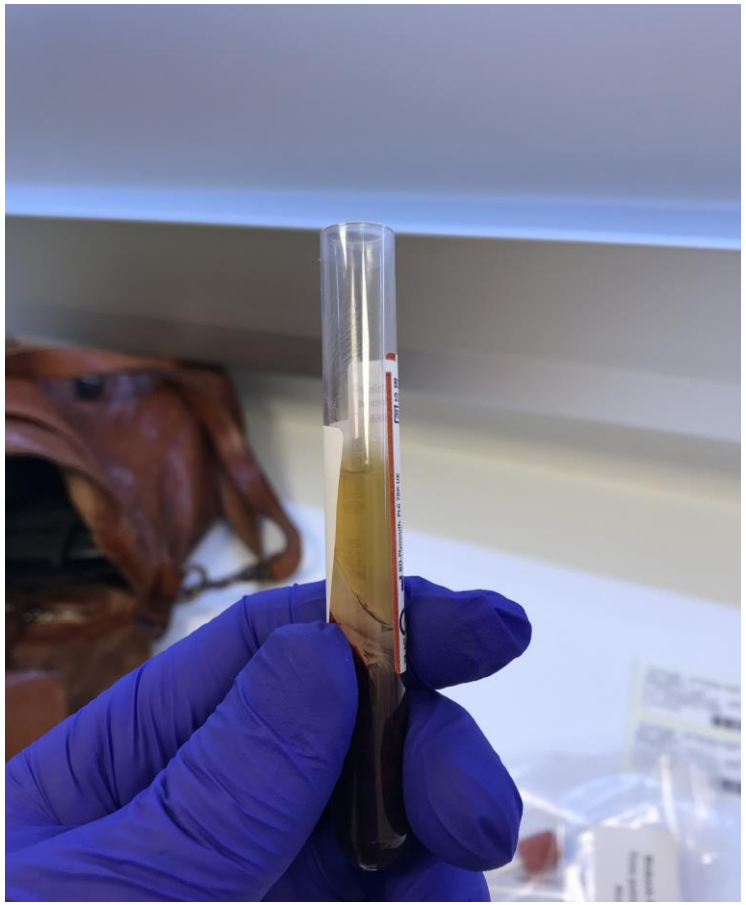


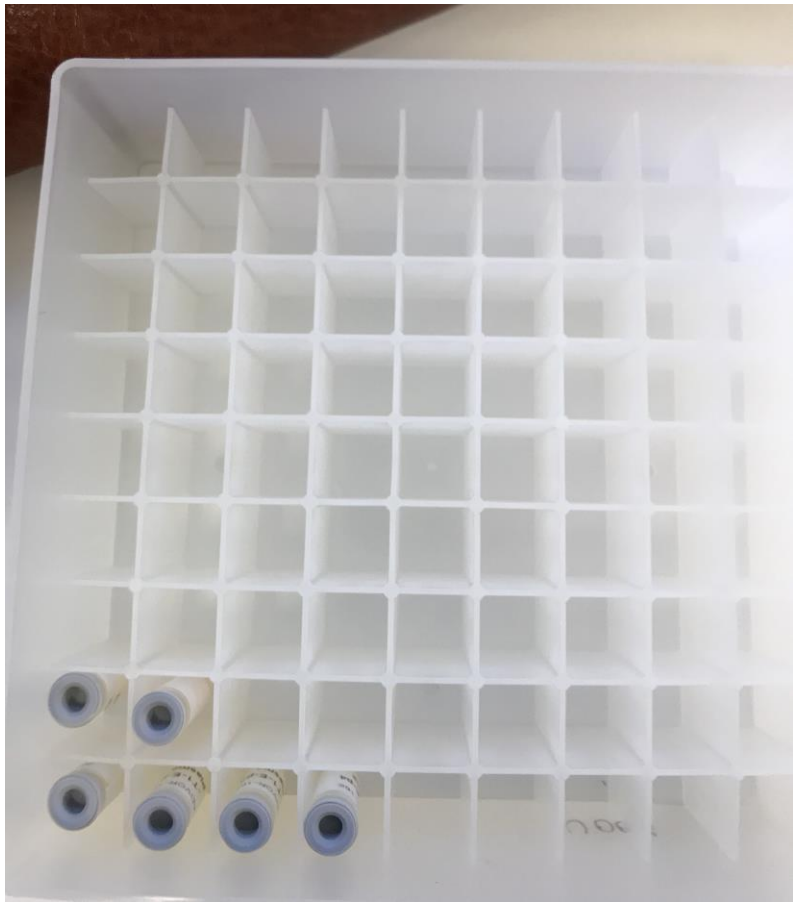
Patient recruitment



Biomarker substudy (February 18, 2020 – 01.05 am)



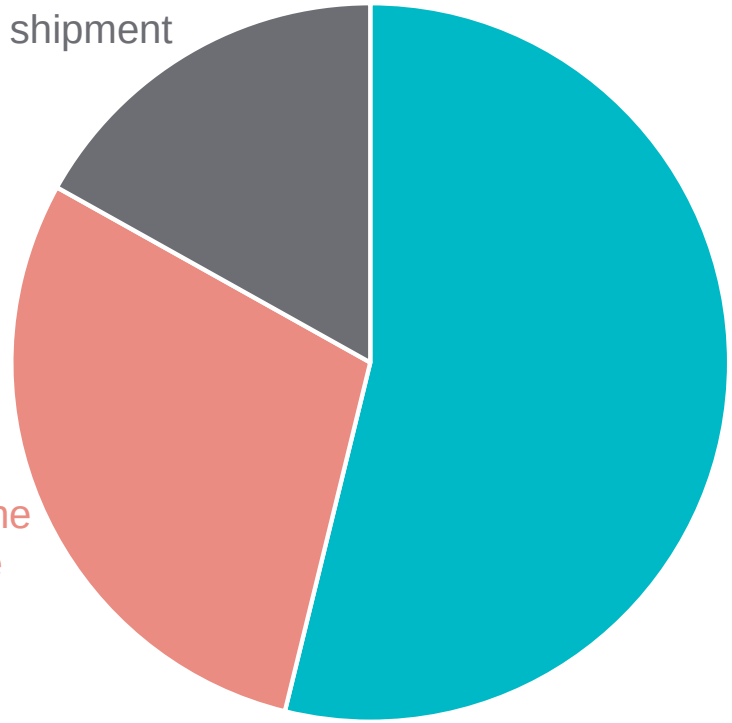




Budget

Total budget of 2,2 million euro (or 2,6 million euro (incl. VAT))

- IMP development
- IMP packaging & shipment
- IVRS (ALEA)
- Statistics



- Project Design and study set-up
- Regulatory and Ethics Review
- Monitoring
- Quality Assurance
- TMF Handling & Administration
- Safety & Endpoint adjudication
- Data Management
- Project Management
- IP management & re-labelling

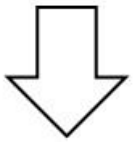
- Study start-up fee/site (29)
- Fee to include patients, to perform the study specific assessments and to enter the collected study data into the clinical study database (CASTOR)

Sponsor ZOL costs Site costs External vendors costs

Methods: congestion score

EDEMA	No edema (score 0)	Trace edema (pitting disappear immediately) (score 1)	Clear pitting edema (score 2)	Visual deformation above ankle (score 3)	Visual deformation above knee (score 4)
PLEURAL EFFUSION (to be confirmed by chest X-ray or ultrasound on admission if suspected)	No pleural effusion (score 0)	Minor (non-amenable for punction) pleural effusion (score 2)		Major (amenable for punction) pleural effusion (score 3)	
ASCITES (to be confirmed by ultrasound on admission if suspected)	No ascites (score 0)	Minor ascites, only detected by echography (score 2)		Significant ascites (score 3)	

Successful decongestion



Continue IV diuretic therapy

Mullens W et al. Eur J Heart Fail. 2018;20:1591-1600

Methods: primary end point

Primary end point:

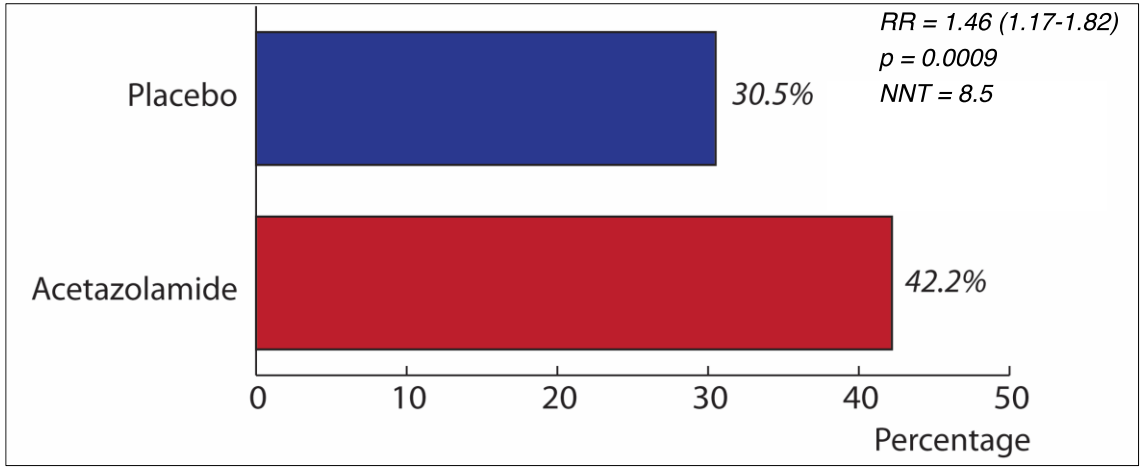
Successful decongestion defined as congestion score ≤1 within 3 days after randomization without an indication for escalation of decongestive therapy

=

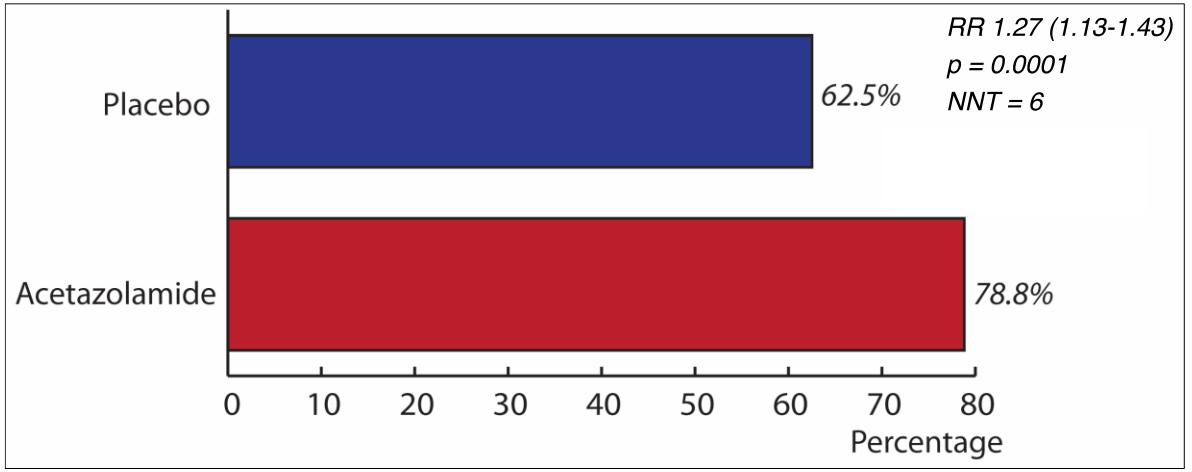
Recommendations	Class[a]	Level[b]
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment.[427,472]	I	C

Mullens W et al. Eur J Heart Fail. 2018;20:1591-1600

Results: successful decongestion



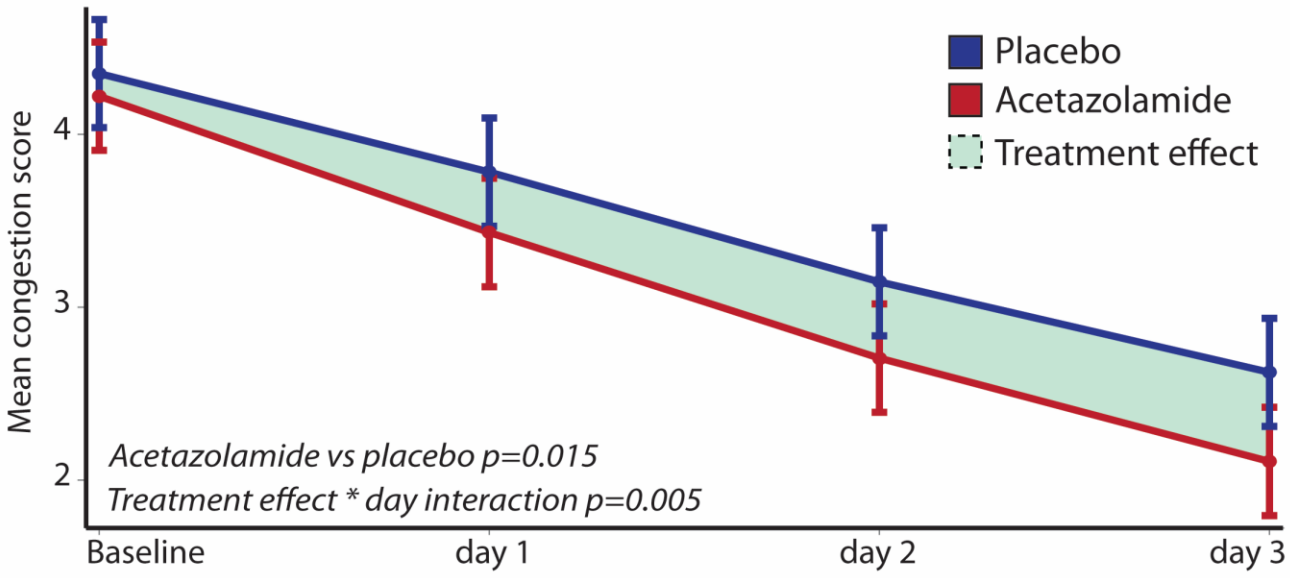
After 3 days (prim endpoint)



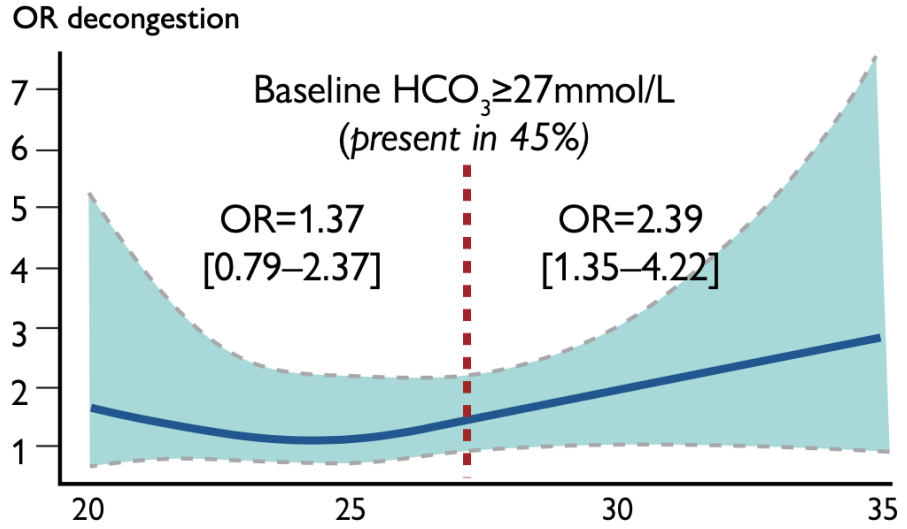
Discharge

Mullens W et al. N Engl J Med 2022;387:1185-1195

Acetazolamide prevents loop diuretic resistance



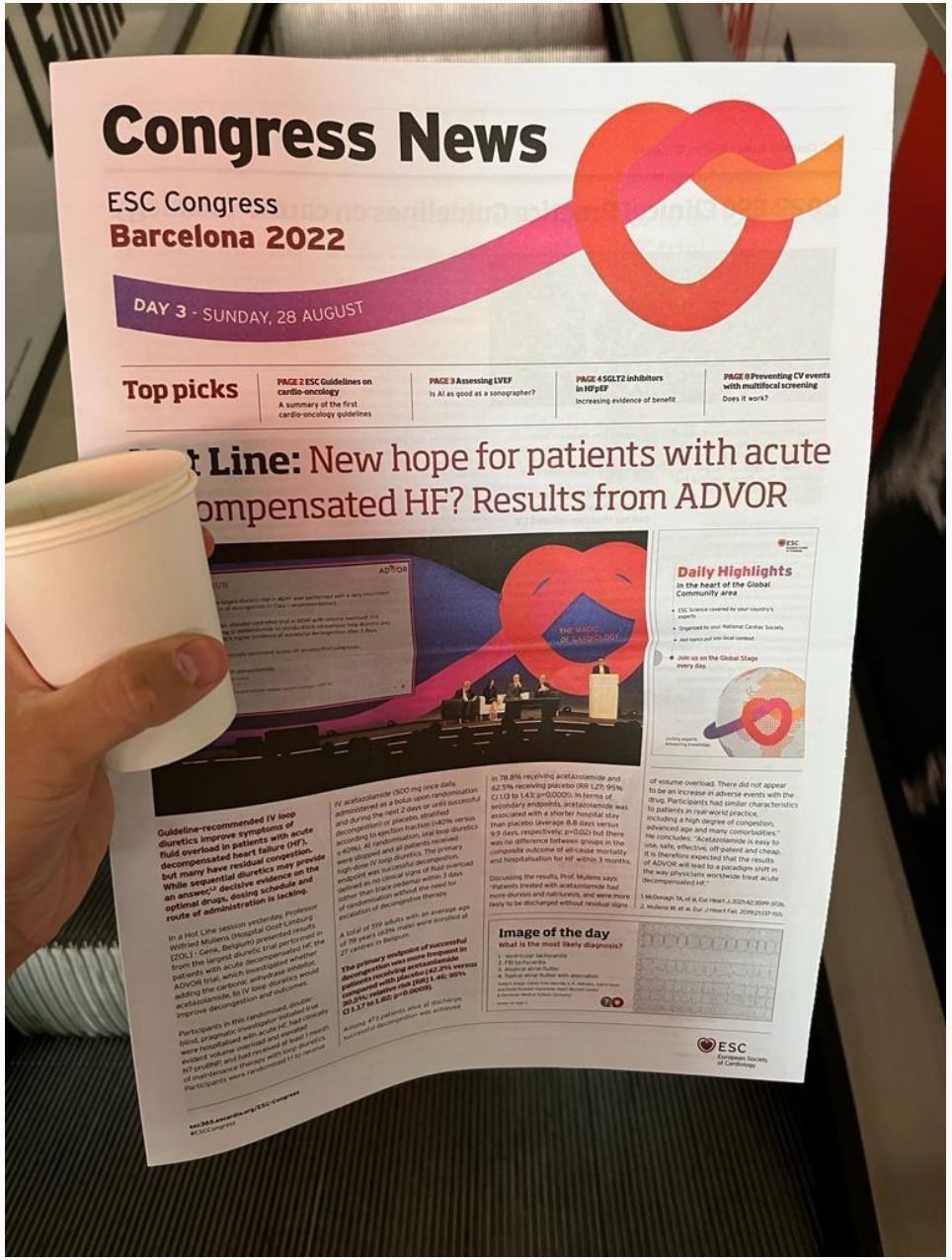
Higher decongestive response, diuresis, natriuresis and shorter LOS if baseline HCO_3 ≥27mmol/L



Mullens W et al. N Engl J Med 2022;387:1185-1195
Martens P, Mullens W et al Eur Heart J 2023; 44:1995-2005.

ADVOR

“door to combo-diuretic time”



Effect of Loop Diuretic Omission in ambulatory HF

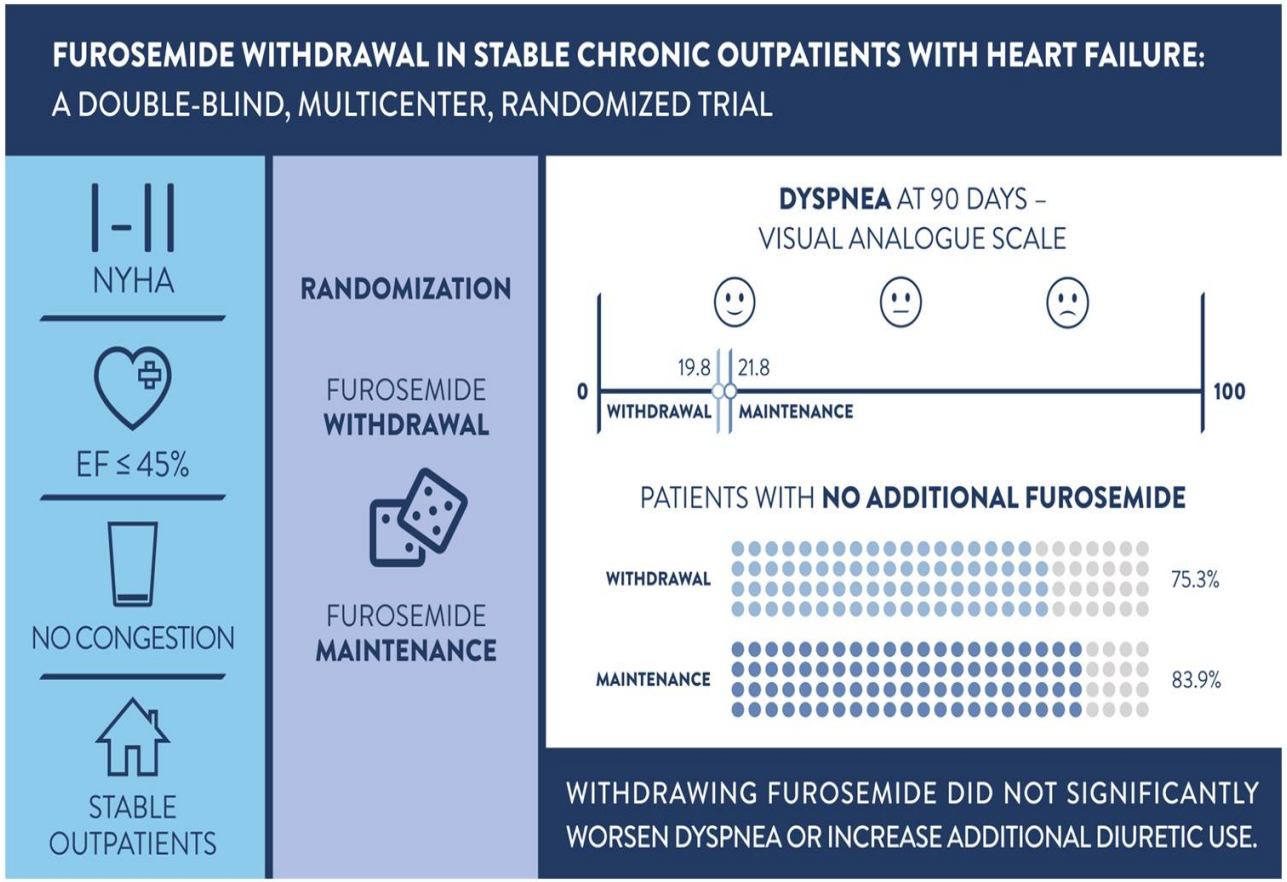
1. No clear guidance in the guidelines

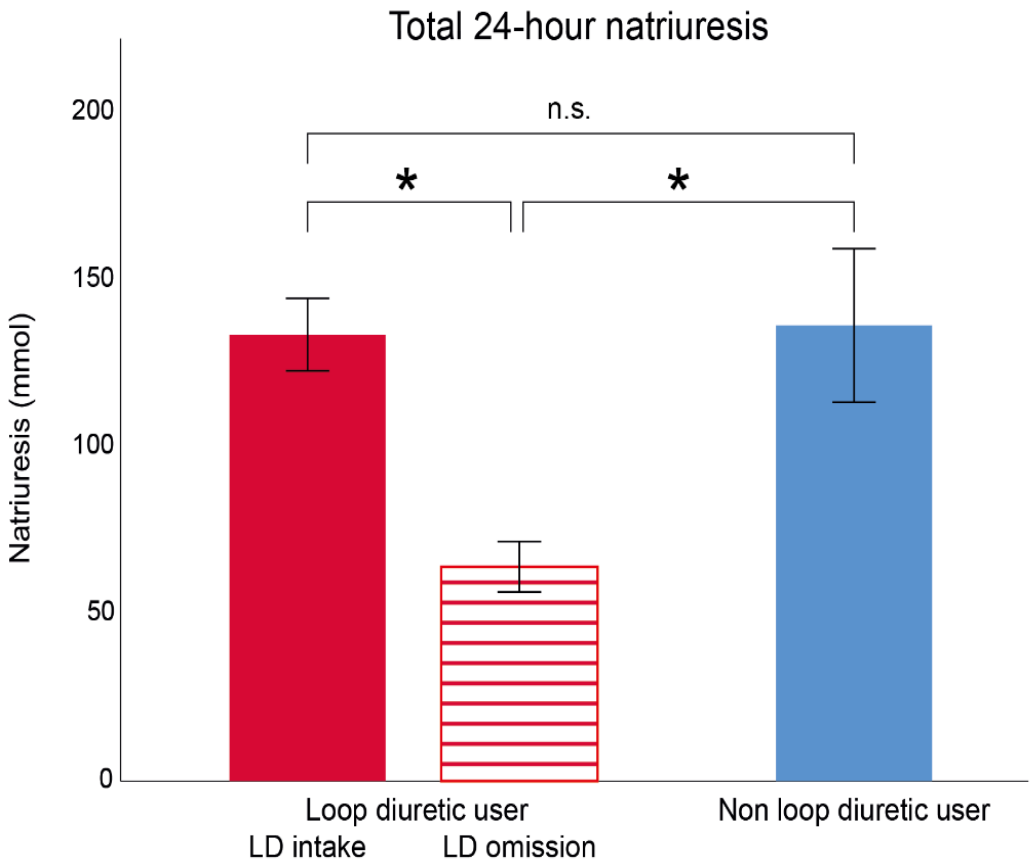
2. Conditions for succesfull downtitration
   - Maximally tolerated dose of GDMT
   - Compliant patient
   - No residual congestion clinically
   - Nml RV function with nml VCI
   - Nml diastolic function
   - NTproBNP < 500

3. Instruct patients on follow-up

4. Future probably through urinary sodium analysis

Effect of Loop Diuretic Omission in ambulatory HF: conflicting data

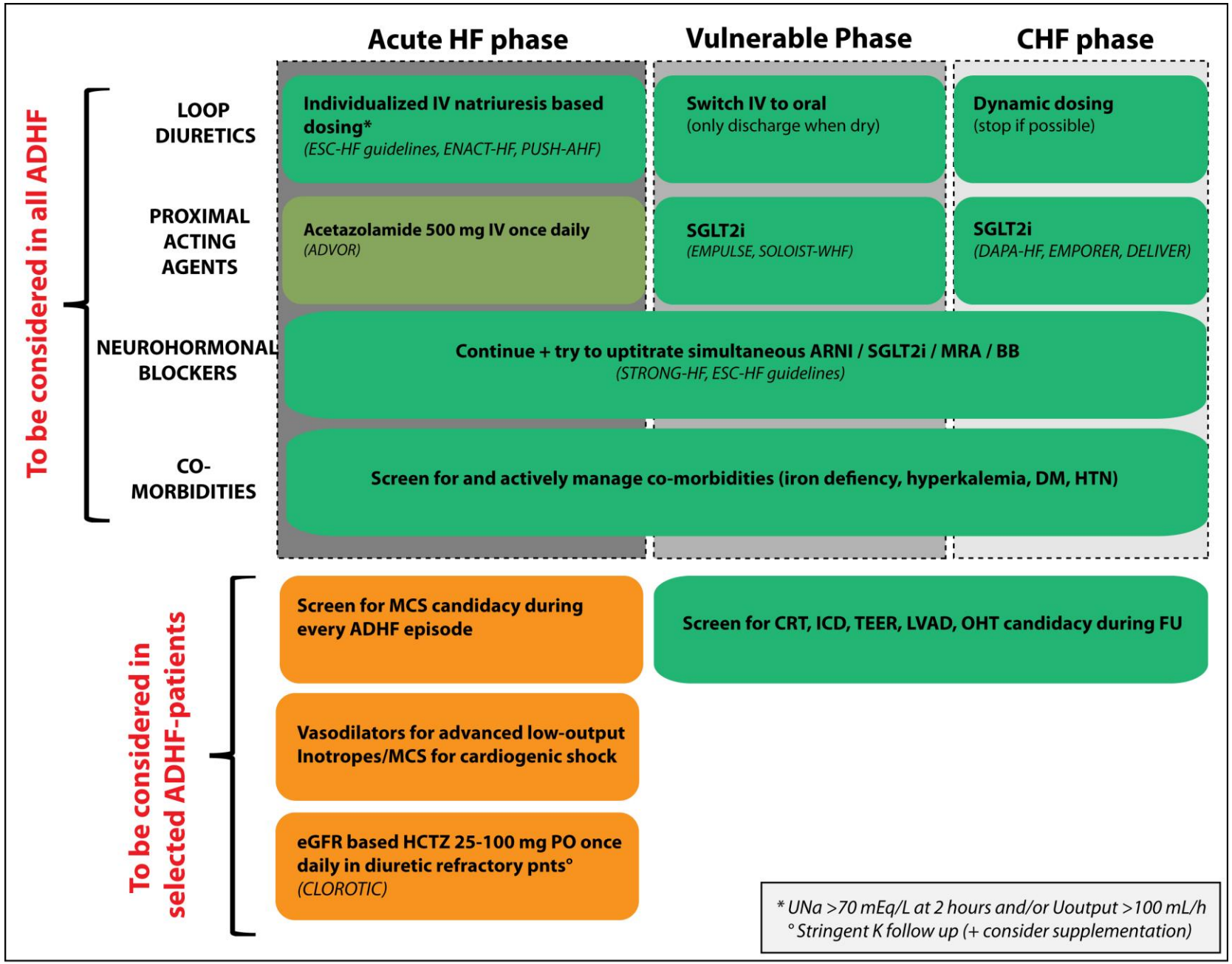




Rohde L et al. Eur Heart J 2019;40:3605–3612
Dauw J, Mullens W. Eur J Heart Fail 2021;23:1110-1119.

Misinterpretation of WRF leads to

- Ineffective decongestion in AHF
- Insufficient dosing of GDMT in CHF



Adapted from Mullens W et al. Eur Heart J 2023;44:2159-2169