Intenstieve strategie bij acuut hartfalen

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Disclosures

- Sprekerskosten betaald aan het UMCG door Novartis, Roche en Boehringer Ingelheim
- Consultancy vergoeding betaald aan het UMCG door Moderna en Novo Nordisk
- Onderzoeksfinanciering van de Hartstichting en NWO (Off Road en Veni)

Casus – 55 jarige man

VG:

2018 Niet-ischemisch HFrEF (EF: 10-15%), stolsel in de LV

Sustained VT's wv ICD implantatie

DM type 2, hypercholesterolemie

Anamnese:

- Laatste weken progressieve dyspnoe d'effort
- Ook sinds enkele dagen orthopnoe
- Enige oedemen
- 6 kg aangekomen
- Vol gevoel; buik voelt boller aan
- Ophogen diuretica door de huisarts geen effect (nu 2 dd 4 mg bumetanide)

Casus – 55 jarige man

Lab:

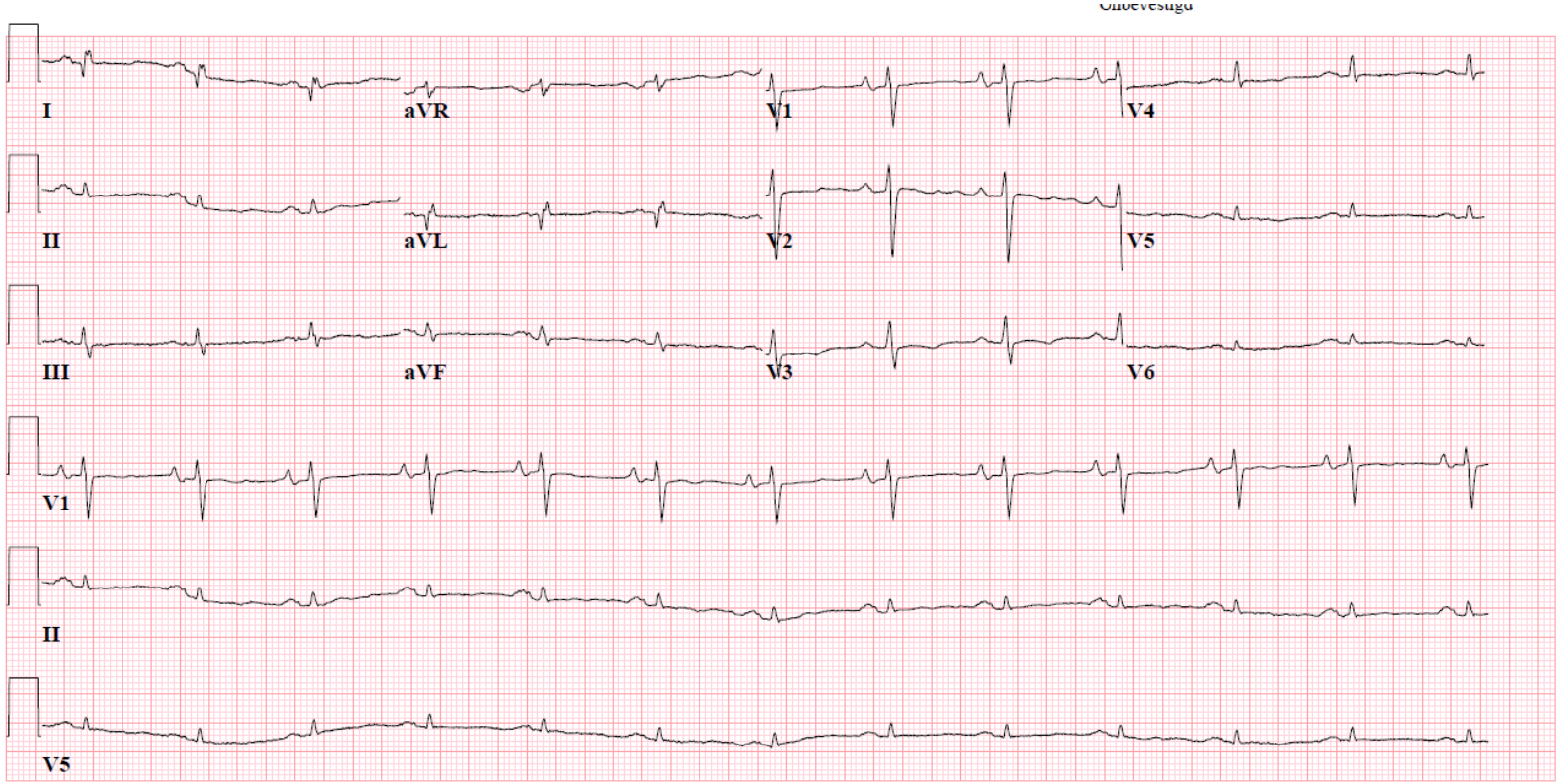
Hb: 6,9

Na: 136

K: 4.8

eGFR: 50

NT-pro-BNP: 2.174

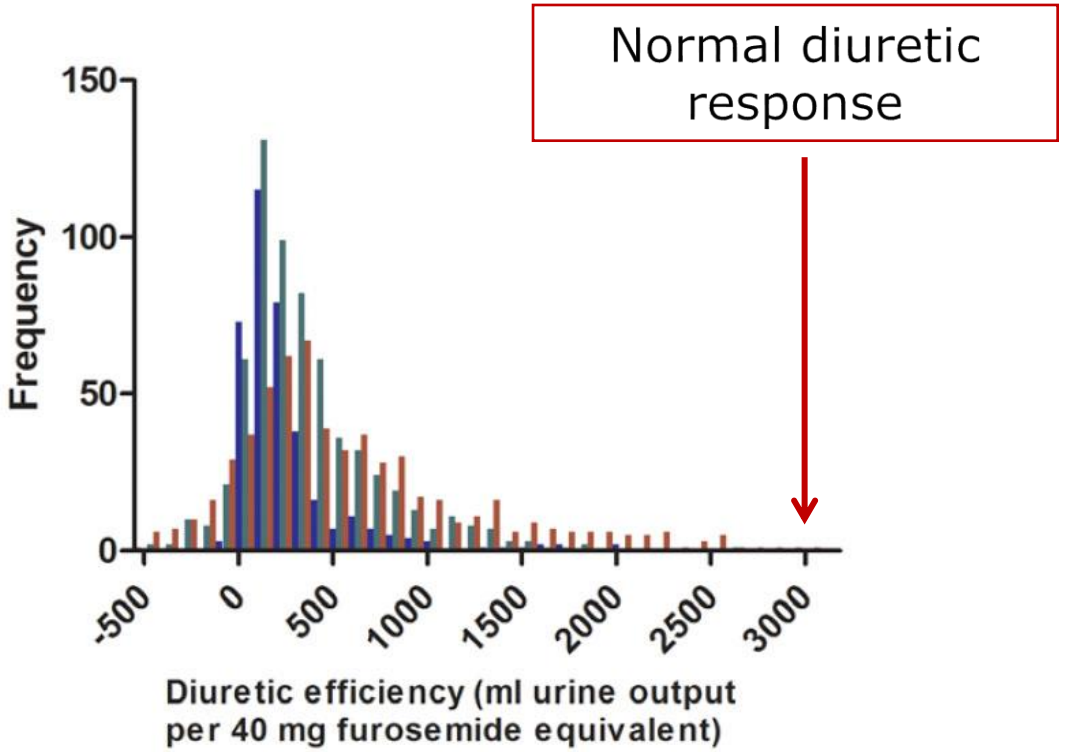


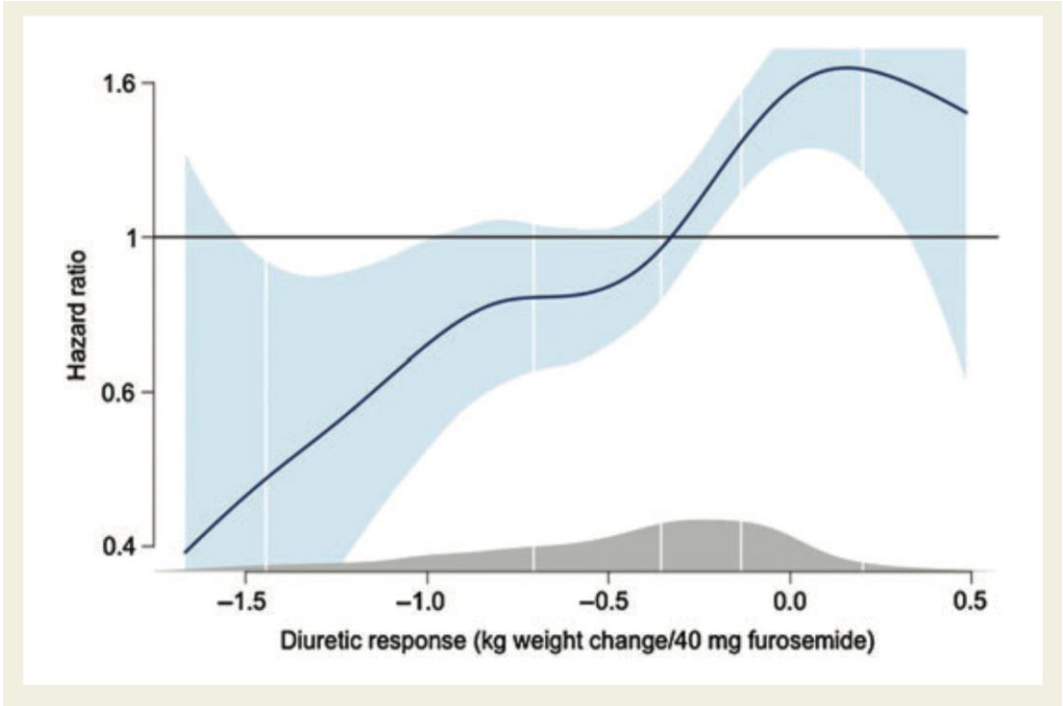
Opname – start iv diuretica

Hoe gaat u het effect hiervan monitoren?

A. Dagelijks wegen/vochtbalans
B. Nierfuntieveranderingen
C. Urine natrium
D. Waarom monitoren?

Diuretische respons





Testani et al. Circ 2014; Valente et al. EHJ 2015

Selectie van (adequate) start dosering

Table 2. Secondary End Points for Each Treatment Comparison.*

End Point	Low Dose (N=151)	High Dose (N=157)	P Value
AUC for dyspnea at 72 hr	4478±1550	4668±1496	0.04
Freedom from congestion at 72 hr — no./total no. (%)	16/143 (11)	28/154 (18)	0.09
Change in weight at 72 hr — lb	−6.1±9.5	−8.7±8.5	0.01
Net fluid loss at 72 hr — ml	3575±2635	4899±3479	0.001
Change in NT-proBNP at 72 hr — pg/ml	−1194±4094	−1882±4105	0.06
Worsening or persistent heart failure — no./total no. (%)	38/145 (26)	34/154 (22)	0.40
Treatment failure — no./total no. (%)†	54/147 (37)	62/155 (40)	0.56
Increase in creatinine of >0.3 mg/dl within 72 hr — no./total no. (%)	20/147 (14)	35/154 (23)	0.04

High dose = 2,5 * de totale orale lisdiuretica dosering thuis

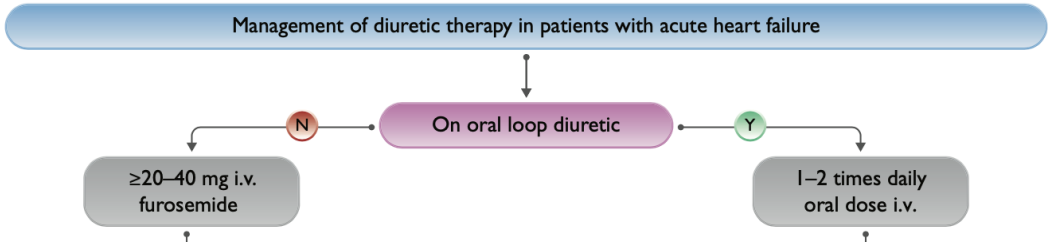


Table 2 Determination of loop diuretic starting dose in all patients

	Loop diuretic naive	Chronic loop diuretic use[a]
eGFR ≥60 ml/min/1.73 m^2	Bolus of 1 mg of bumetanide	Bolus equal to total daily loop diuretic dose at home[b]
eGFR <60 ml/min/1.73 m^2	Bolus of 2 mg of bumetanide	Bolus double the total daily loop diuretic dose at home[b]

Maintenance dose is twice daily bolus dose

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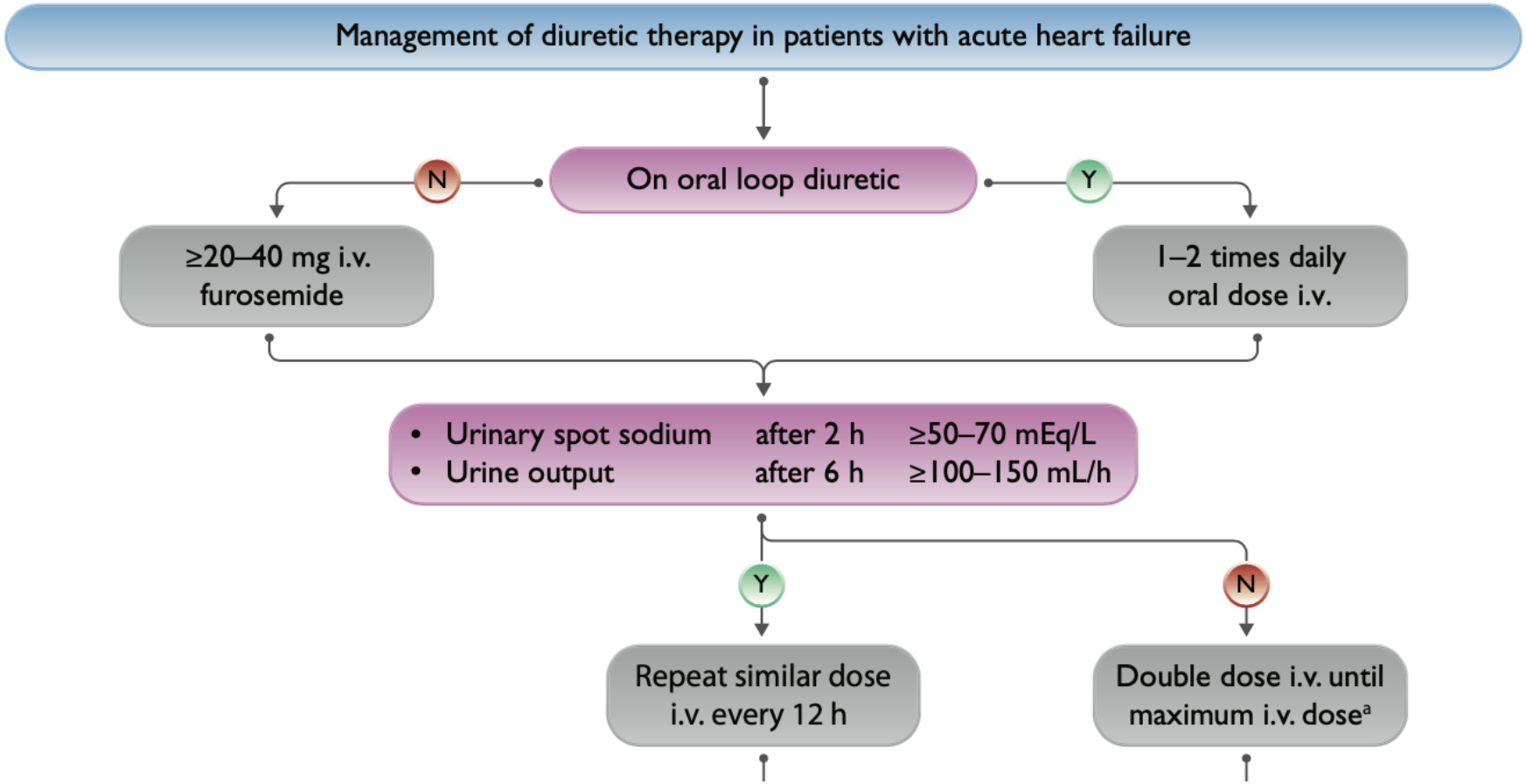
Felker et al. NEJM 2011; McDonagh et al. EHJ 2021; ter Maaten et al. EJHF 2022

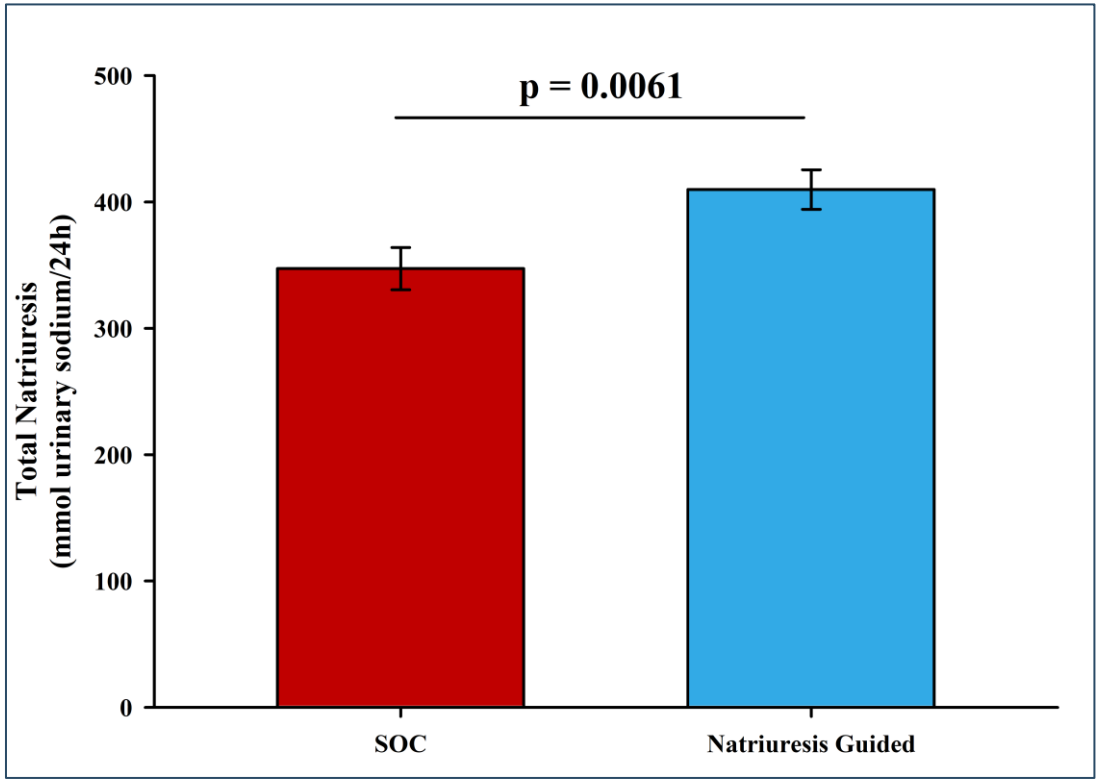
Behandeling van AHF in de HF richtlijn



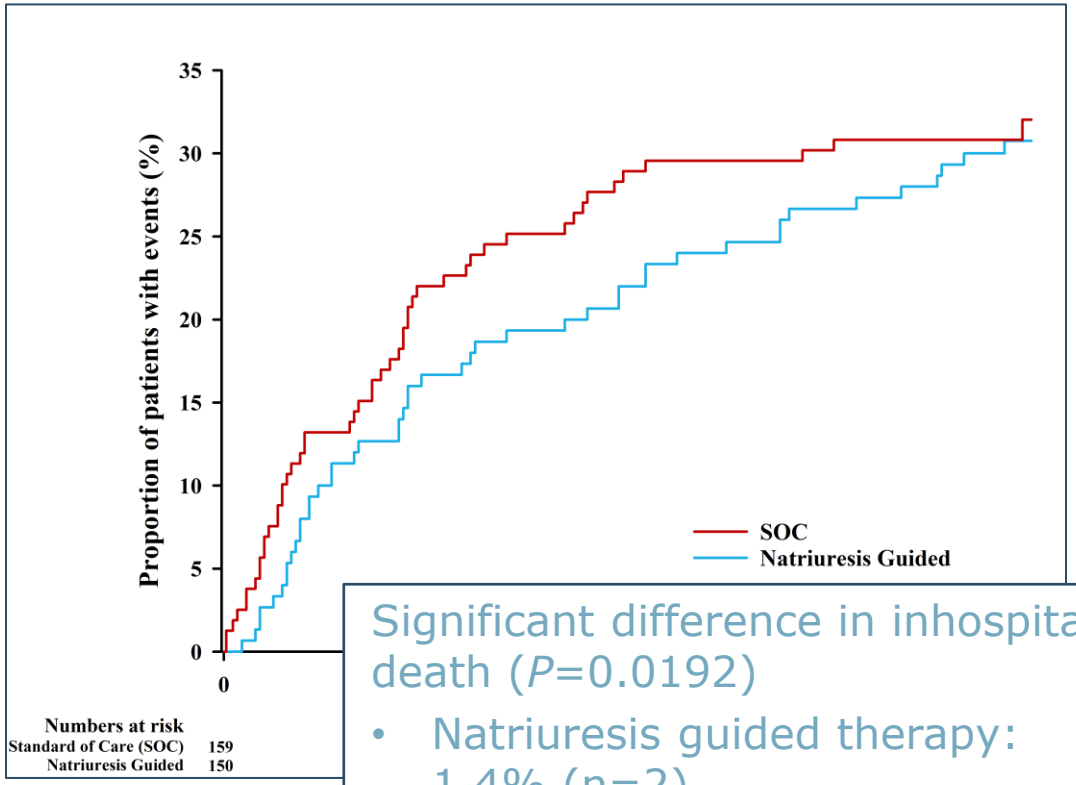
McDonagh et al. EHJ 2021

Dual primary endpoint

24-hours natriuresis



180 days ACM & HF hosp



Significant difference in inhospital death (*P*=0.0192)

- Natriuresis guided therapy: 1.4% (n=2)
- Standard of care: 7.5% (n=12)

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ter Maaten et al. Nat Med 2023

Terug naar de casus

Start dosering bumetanide 2 dd 5 mg iv

PUSH protocol

T=0: uNa 75

T=2: uNa 69, extra bolus Burinex.

T=6: uNa 74, diurese >150 cc/uur

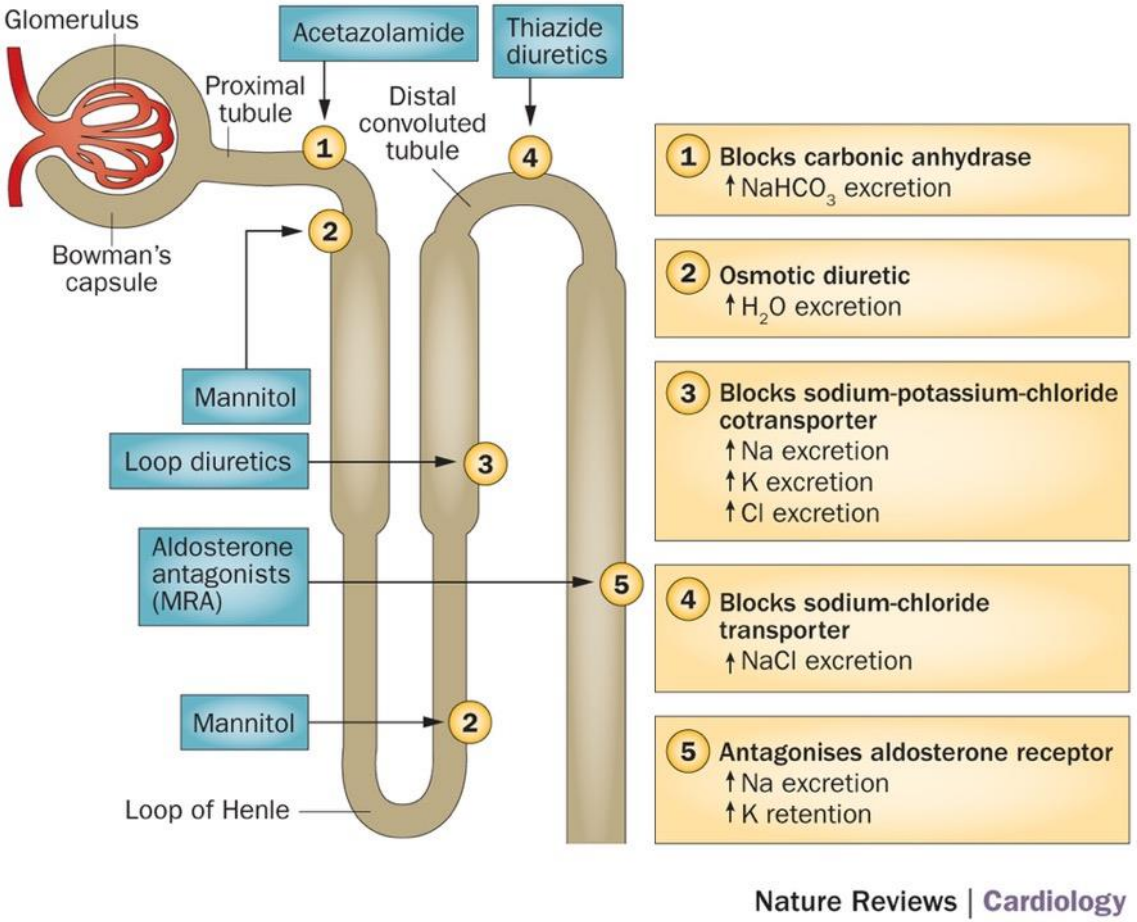
T=12: uNa 66, extra bolus Burinex.

T=18: uNa 60

Hoe verder?

A. Extra bumetanide
B. Combinatie diuretica therapie
C. Ultrafiltratie
D. Onveranderd zo door

Onvoldoende respons – wat nu?



Werkt 'niet':

- Spironolacton (ATHENA HF)
- Dopamine (ROSE en DAD HF)
- Rolofylline (PROTECT)
- Nesiritide (ROSE en ASCEND HF)
- Serelaxine (RELAX 2)
- Ularitide (TRUE)

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ter Maaten et al. Nat Rev Cardiol 2015

HCT – CLOROTIC trial

Study population

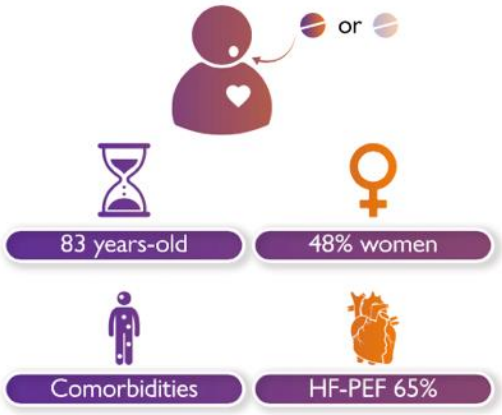
Randomized, double-blind, placebo-controlled clinical trial

History of chronic heart failure

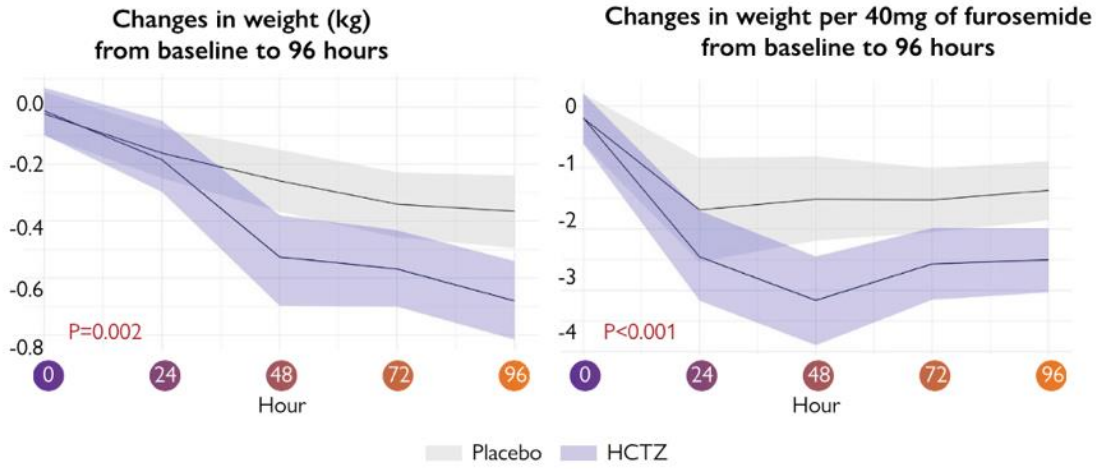
Treatment with oral furosemide (80-240 mg/day)

Admission for acute decompensation

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



Efficacy



Safety	Placebo	HCTZ	p-value
All-cause mortality at 90 days	19 (16.4%)	23 (20.2%)	0.566
All-cause rehospitalizations at 90 days	40 (34.5%)	43 (37.7%)	0.709
Impaired renal function (serum creatinine and eGFR)	20 (17.2%)	53 (46.5%)	<0.001
Hyponatraemia (Na+ ≤ 130 mmol/L) - (Na+ ≤ 125 mmol/L)	6 (5.2%)–2 (1.7%)	10 (8.8%)–3 (2.6%)	0.416–0.682
Hypokalaemia (K+ ≤ 3.0 mmol/L) - (K+ ≤ 2.5 mmol/L)	18 (16.1%)–0 (0.0%)	43 (40.6%)–2 (1.8%)	<0.001–0.245
Serious adverse events	27 (23.3%)	26 (22.8%)	0.93

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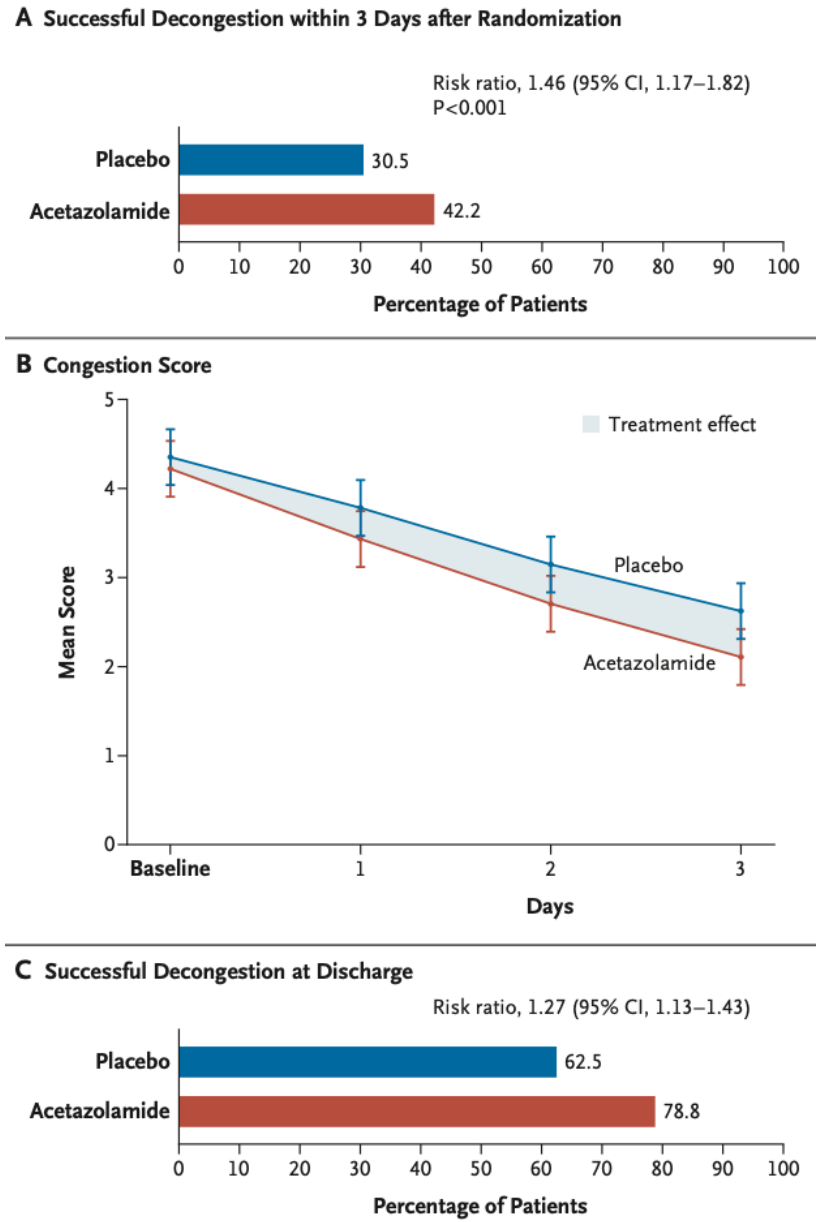
Trullas et al. Eur Heart J 2022

Acetazolamide – ADVOR trial

519 patiënten met AHF
1:1 acetazolamide:placebo

Primaire eindpunt: succesvolle decongestie binnen 3 dagen zonder escalatie therapie

Adverse events				
During treatment phase — no. (%)				
Combined renal safety end point	2 (0.8)	7 (2.7)	—	0.10
Doubling of serum creatinine level from baseline	0	2 (0.8)	—	0.24
≥50% sustained decrease in estimated GFR	1 (0.4)	4 (1.6)	—	0.21
Renal-replacement therapy during index hospitalization	1 (0.4)	4 (1.6)	—	0.21
Severe metabolic acidosis¶	0	0	—	—
Hypokalemia‖	10 (3.9)	14 (5.5)	—	0.39
Hypotension**	9 (3.5)	17 (6.6)	—	0.11
During 3 mo of follow-up — no. (%)				
Serious adverse event	124 (47.9)	123 (48.0)	—	1.00
Adverse event related to placebo or acetazolamide	3 (1.2)	8 (3.1)	—	0.14
Cardiovascular adverse event	122 (47.1)	113 (44.1)	—	0.53



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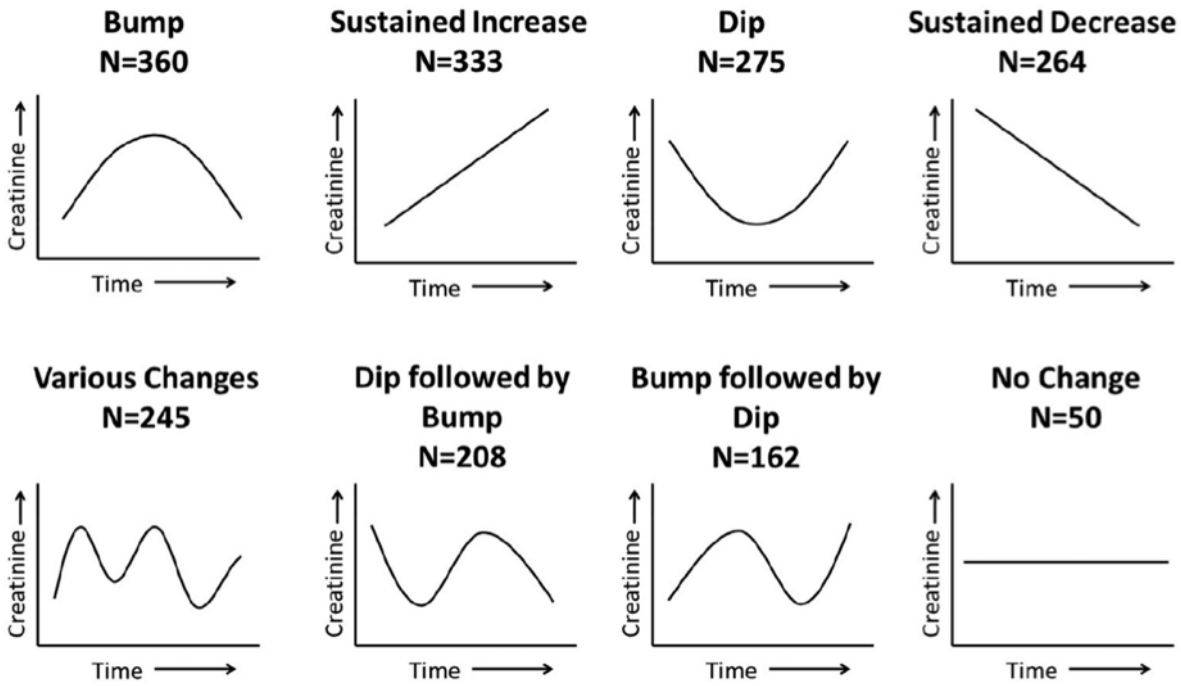
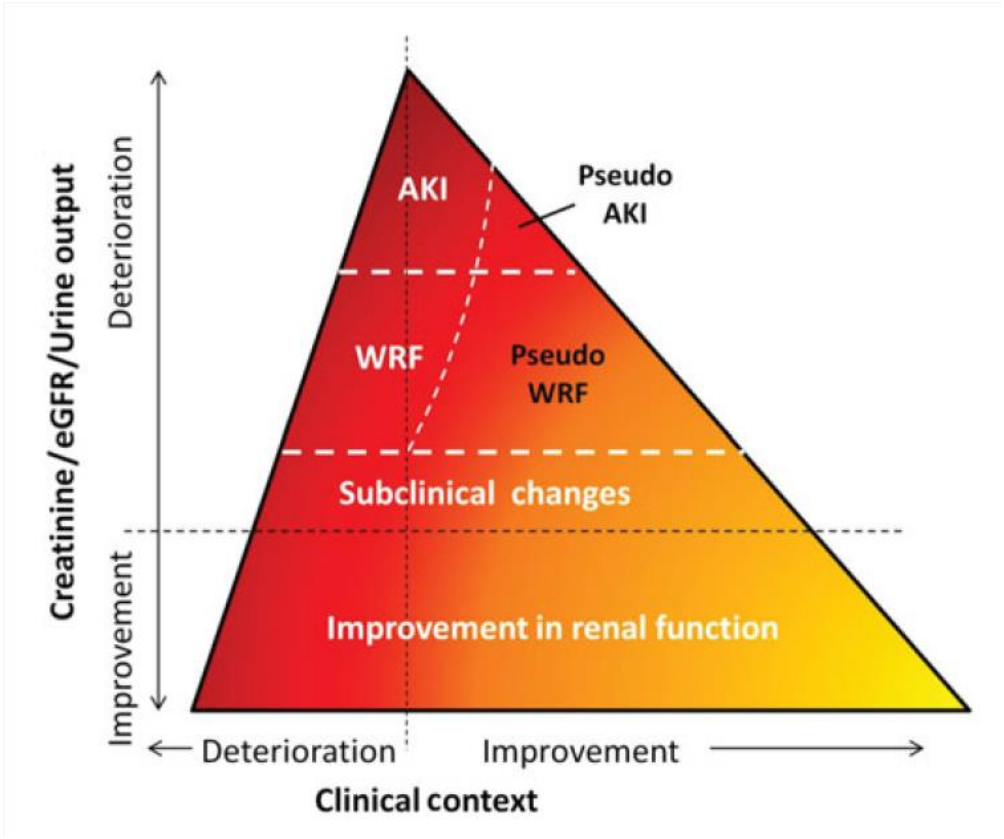
Mullens et al. NEJM 2022

Nierfunctie tijdens decongestie





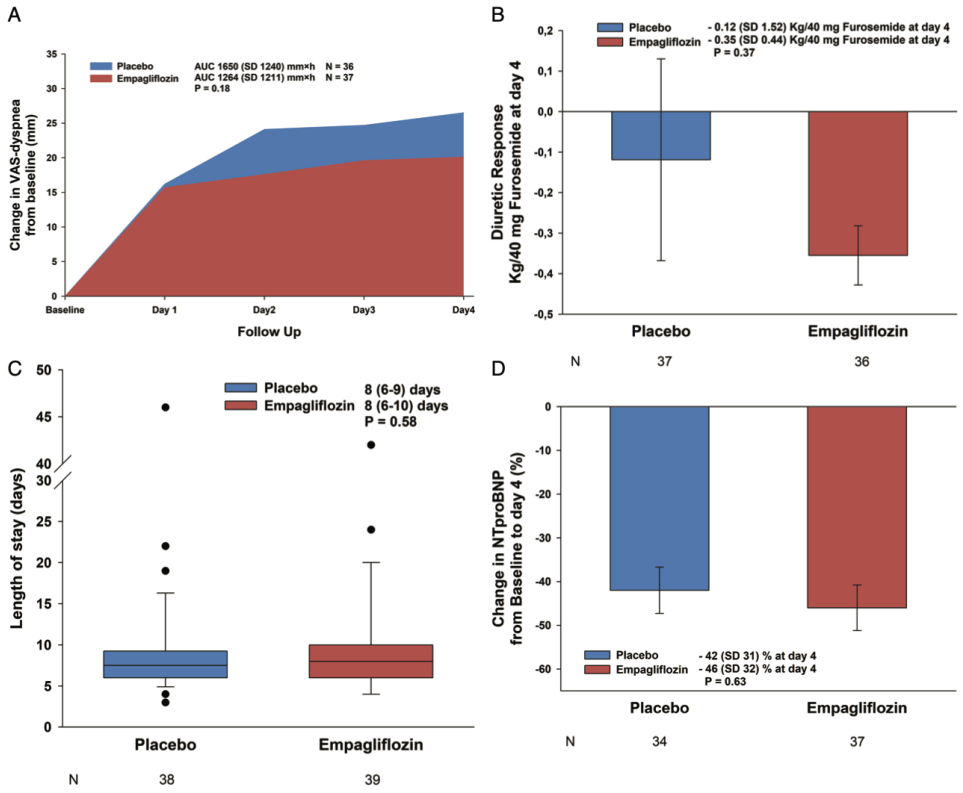
Beldhuis et al. JCF 2018; Damman et al. EHJ 2015

Hoe gaat u om met de hartfalenmedicatie tijdens opname?

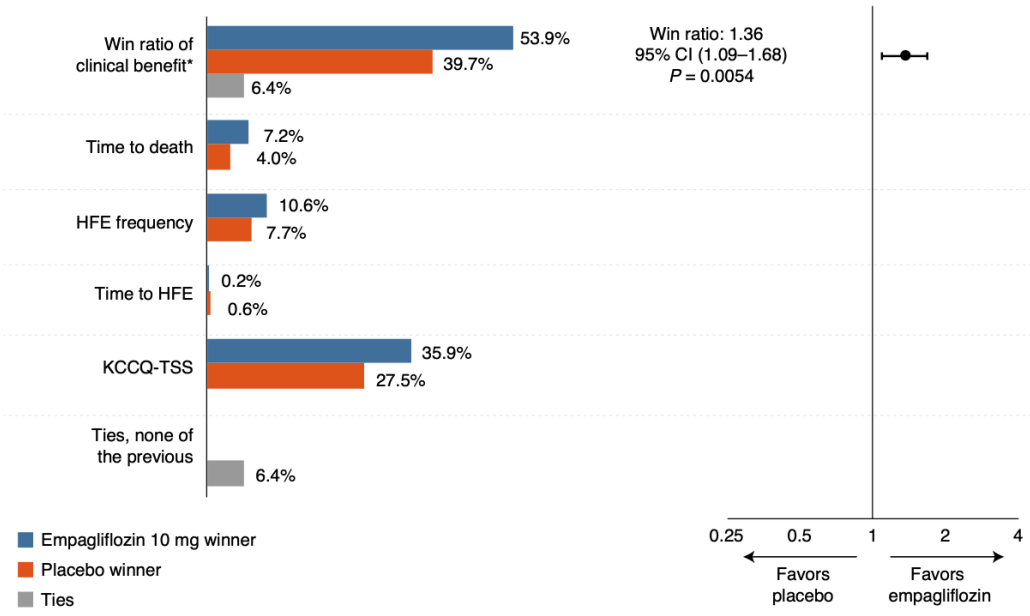
A. Ik start zo snel mogelijk met alle hartfalenmedicatie
B. Ik start zo snel mogelijk met een deel van de medicatie
C. Ik ben terughoudend en wil eerst kijken hoe het gaat
D. Ik probeer de hartfalenmedicatie te starten voor ontslag

Vroege initiatie van GDMT

EMPA RESPONSE trial



EMPULSE trial



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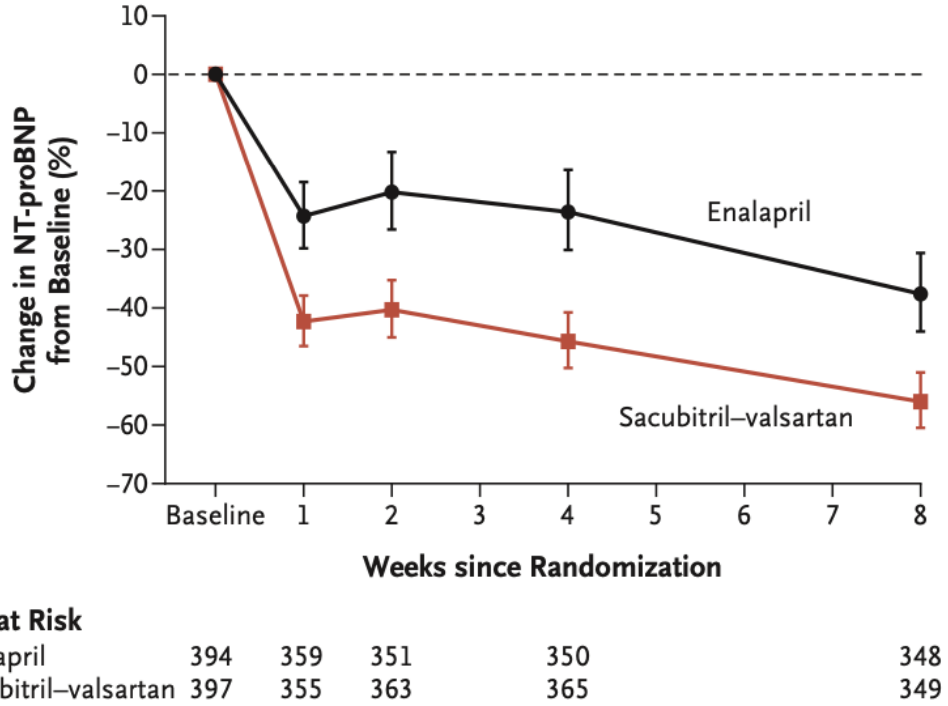
Damman et al. EJHF 2020; Voors et al. Nat Med 2022

Initiatie in het ziekenhuis

PIONEER HF trial



ATHENA trial

Table 3. Changes in Serum Potassium Concentration and Renal Function

Change	Median (25th-75th) Usual Care Alone	Median (25th-75th) High-Dose Spironolactone	Mean (SD) Usual Care Alone	Mean (SD) High-Dose Spironolactone	*P* Value
Change in Serum Potassium, mEq/L (to Convert to Millimoles per Liter, Multiply by 1.0)					
24-h	0.00 (−0.40 to 0.30)	0.00 (−0.30 to 0.30)	0.01 (0.56)	−0.00 (0.47)	.50
48-h	0.10 (−0.30 to 0.40)	0.10 (−0.10 to 0.40)	0.04 (0.52)	0.16 (0.46)	.02
72-h	0.20 (−0.40 to 0.55)	0.20 (−0.20 to 0.60)	0.09 (0.62)	0.22 (0.52)	.08
96-h	0.20 (−0.30 to 0.60)	0.30 (0.00 to 0.70)	0.15 (0.69)	0.31 (0.54)	.08
Change in Serum Creatinine, mg/dL (to Convert to Micromoles per Liter, Multiply by 88.4)					
24-h	0.05 (−0.05 to 0.20)	0.05 (−0.03 to 0.17)	0.07 (0.18)	0.06 (0.17)	.76
48-h	0.02 (−1.10 to 0.20)	0.10 (−0.03 to 0.02)	0.10 (0.27)	0.09 (0.20)	.67
72-h	0.08 (−0.08 to 0.22)	0.10 (−0.03 to 0.28)	0.13 (0.33)	0.12 (0.26)	.85
96-h	0.10 (−0.02 to 0.33)	0.10 (−0.05 to 0.27)	0.16 (0.30)	0.15 (0.30)	.77
Change in Estimated Glomerular Filtration Rate, mL/min/1.73 m^2					
24-h	−1.95 (−8.46 to 2.79)	−2.58 (−7.83 to 1.53)	−2.75 (9.43)	−2.54 (10.80)	.87
48-h	−1.59 (−9.65 to 3.71)	−4.12 (−8.87 to 1.89)	−3.34 (12.52)	−3.33 (11.15)	.95
72-h	−3.70 (−12.06 to 4.09)	−3.71 (−10.67 to 0.87)	−4.47 (13.37)	−4.53 (12.05)	.82
96-h	−5.53 (−13.11 to 0.79)	−4.35 (−11.06 to 1.74)	−5.56 (13.85)	−4.13 (11.58)	.56

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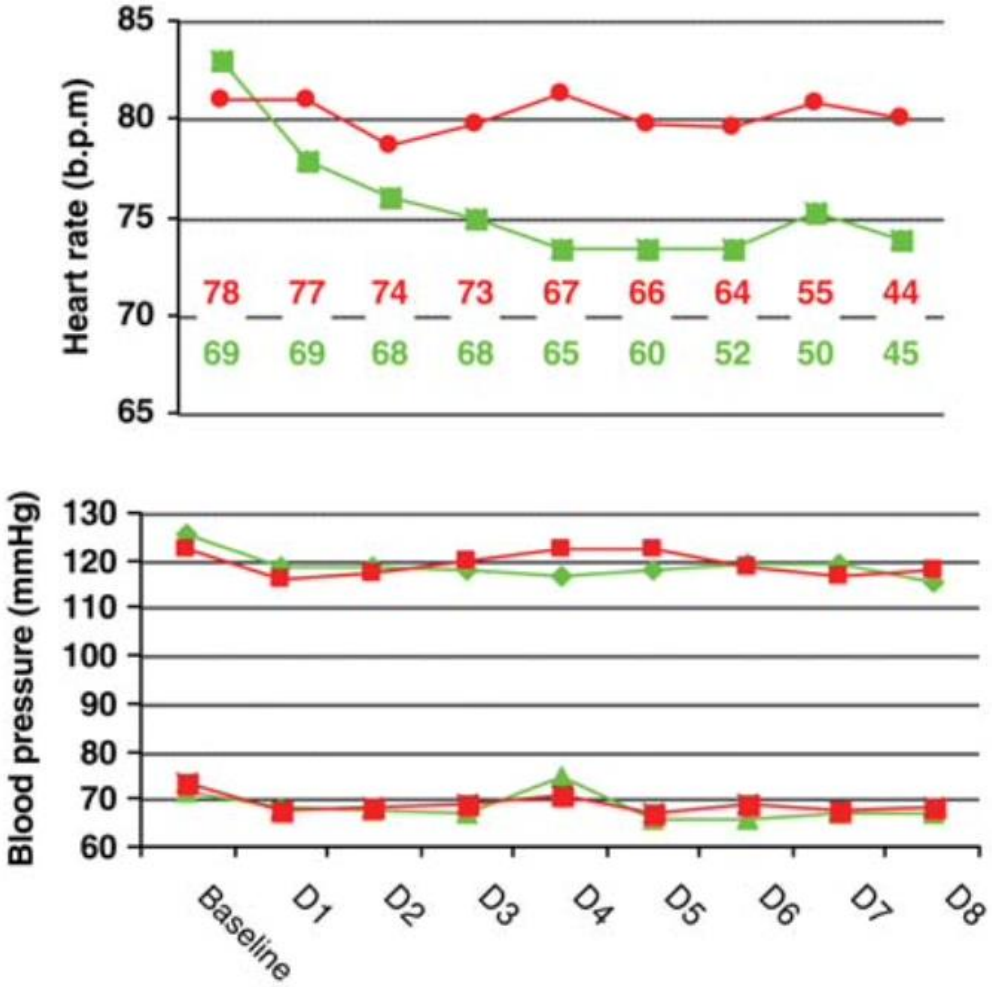
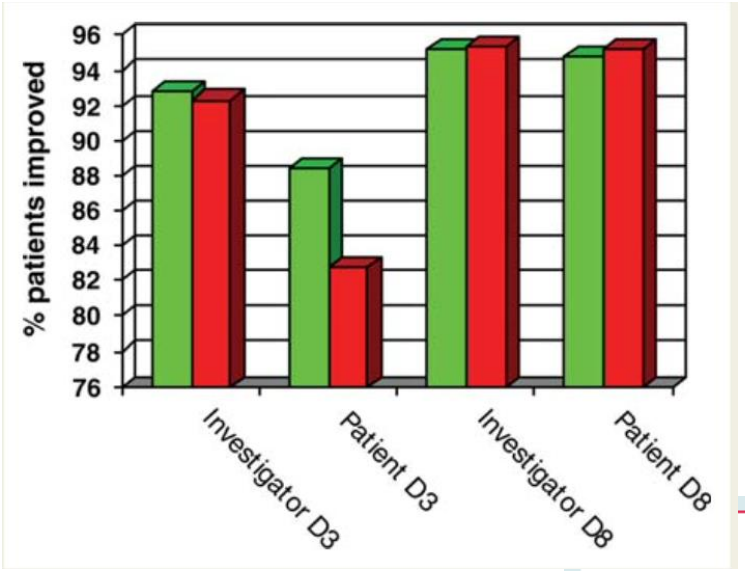
Velazquez et al. NEJM 2018; Butler et al. JAMA Cardiology 2017

Bètablokker staken tijdens AHF opname?



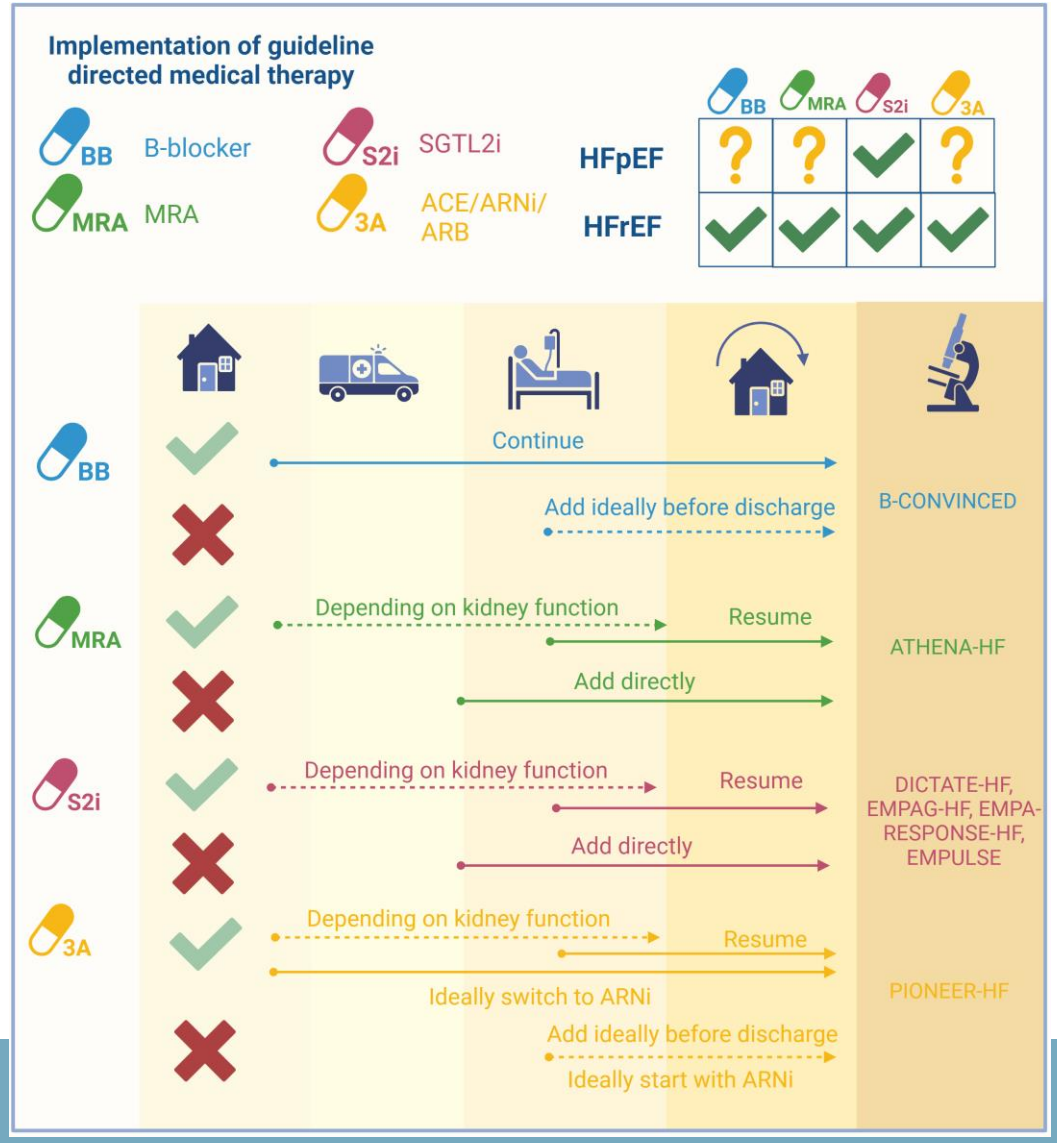


	Keep BB, *n* = 69	Stop BB, *n* = 78	*P*-value
During hospitalization			
Durations (days)	11.5 ± 8.3	10.4 ± 9.7	0.2
Median, range	9 (1–50)	8 (1–62)	
Deaths (n)	1 (HF)	2 (HF)	
Dobutamine (*n*)	3	1	
After 3 months			
Deaths, *n* (%)	6 (9)	6 (8)	0.83
Rehospit, *n* (%)	27 (40)	36 (47)	0.43
For HF	15 (22)	24 (32)	0.19
For arrhythmia	2 (3)	3 (4)	1
Receiving BB, *n* (%)	61 (90)	58 (76)	0.04

Rehospit, rehospitalization; HF, heart failure; BB, beta-blocker.

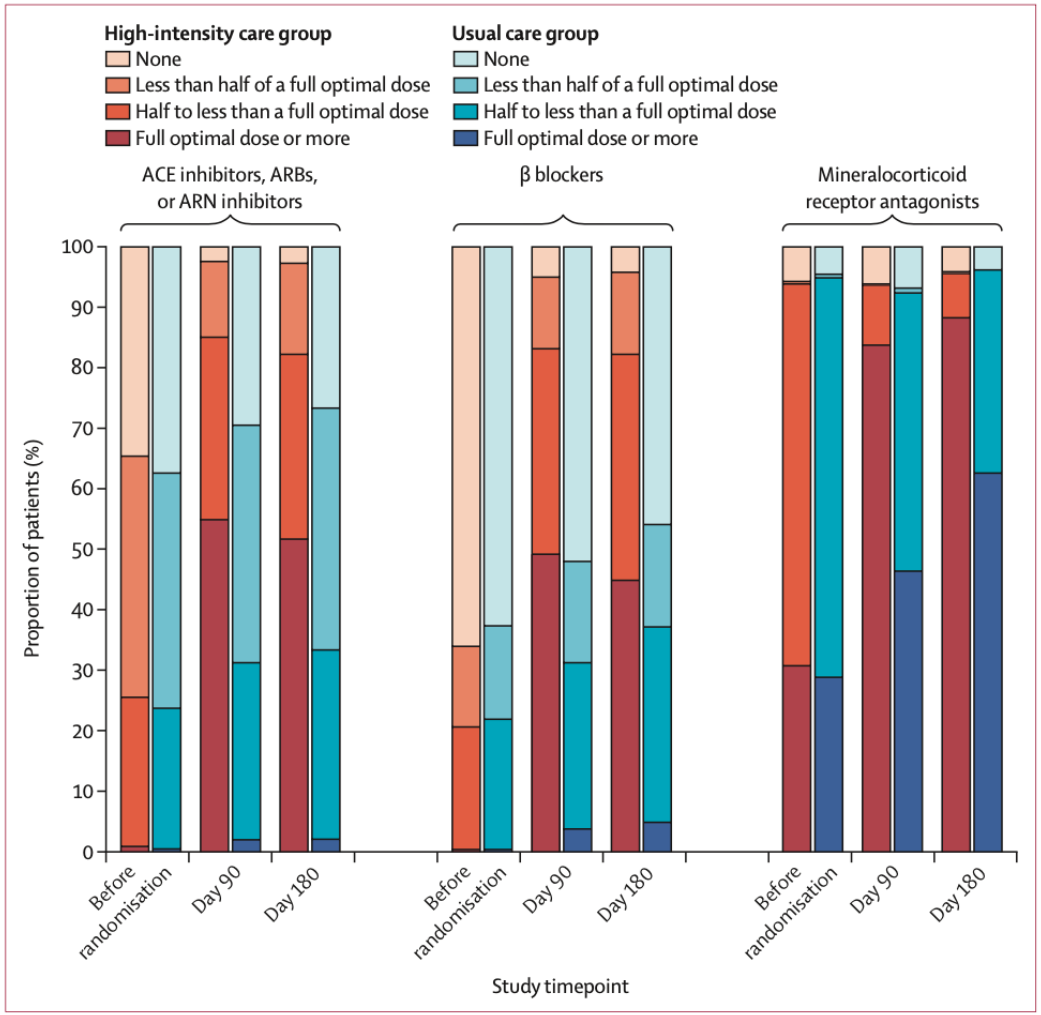
Jondeau et al. EHJ 2009

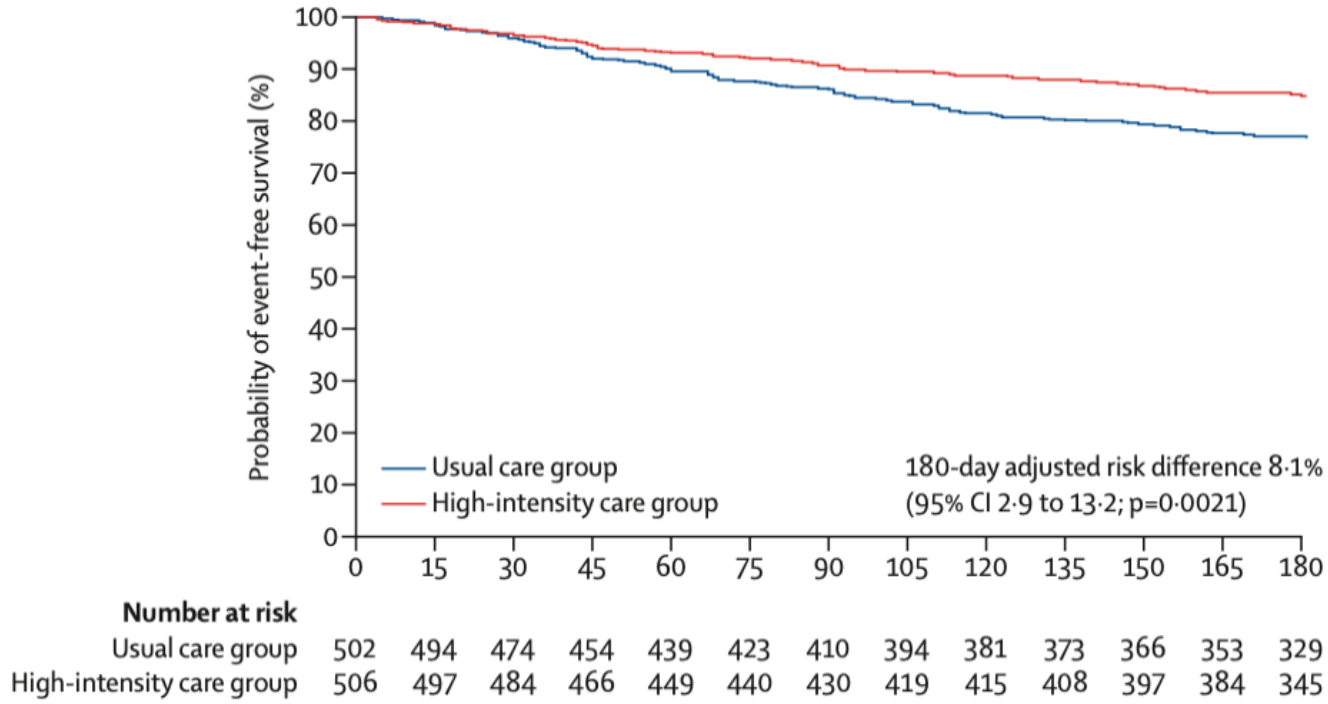
Initiatie van GDMT in het ziekenhuis



Zonneveld et al. Submitted

Resultaten STRONG-HF





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Mebazaa et al. Lancet 2022

Safety indicators voor optitratie in STRONG HF

	Up-titration		Pause uptitration
β blockers	↘ NT-proBNP And HR ≥ 55 bpm And SBP ≥ 95 mmHG	↔ NT-proBNP	↗ NT-proBNP > 10%* Or HR < 55 bpm Or SBP < 95 mmHG
ACEi ARB ARNi MRA	SBP ≥ 95 mmHg And K+ ≤ 5.0 mmol/L And eGFR ≥ 30 mL/min/1.73m^2		SBP < 95 mmHg Or K+ > 5.0 mmol/L Or eGFR < 30 mL/min/1.73m^2
Loop diuretics	↗ NT-proBNP > 10%* Or Congestion assessed by physical examination		↘ NT-proBNP And no congestion assessed by physical examination

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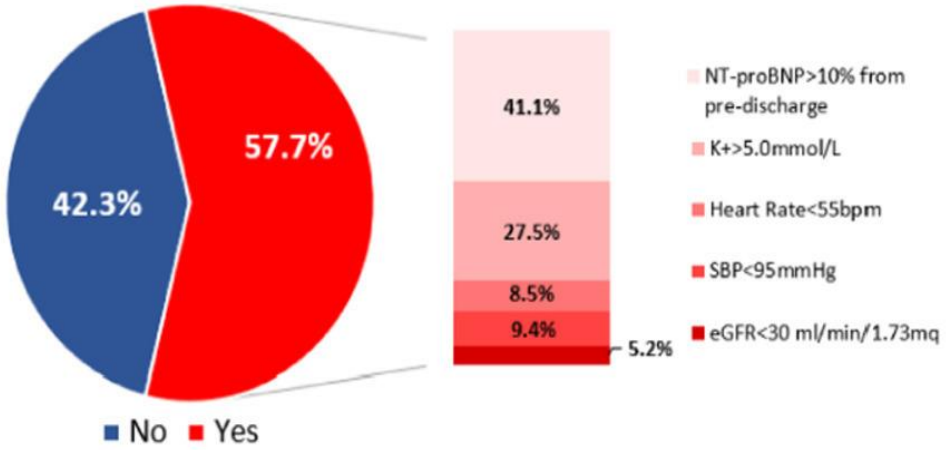
Mebazaa et al. Lancet 2022

Hoe zag dit er in de studie uit?

Study population
542 patients receiving HIC after admission for AHF in STRONG-HF

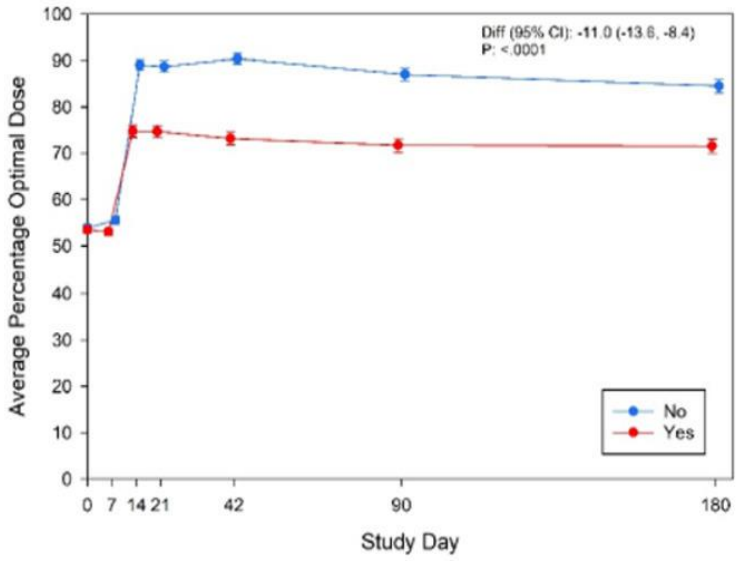
Safety indicators for up-titration of GDMT



Outcome

Safety indicator	Adjusted HR (95%CI) for 180-day all-cause death or HFH
Any indicator	0.84 (0.48, 1.46)
eGFR < 30ml/min/1.73m2	2.06 (0.77, 5.53)
SBP<95mmHg	1.38 (0.51, 3.71)
Heart Rate<55bpm	0.19 (0.03, 1.41)
K+>5.0mmol/L	0.90 (0.49, 1.66)
Δ NT-proBNP >10%	0.83 (0.46, 1.48)

Average Percentage of GDMT Optimal Dose



Group	V2: Day 0	V3: Day 7	V4: Day 14	V5: Day 21	V6: Day 42	V7: Day 90	V8: Day 180
No	53.9 (0.72)	55.5 (0.84)	89.0 (1.18)	88.7 (1.22)	90.4 (1.18)	87.0 (1.29)	84.5 (1.41)
Yes	53.4 (0.70)	53.0 (0.79)	74.8 (1.29)	74.7 (1.33)	73.2 (1.36)	71.7 (1.47)	71.5 (1.50)

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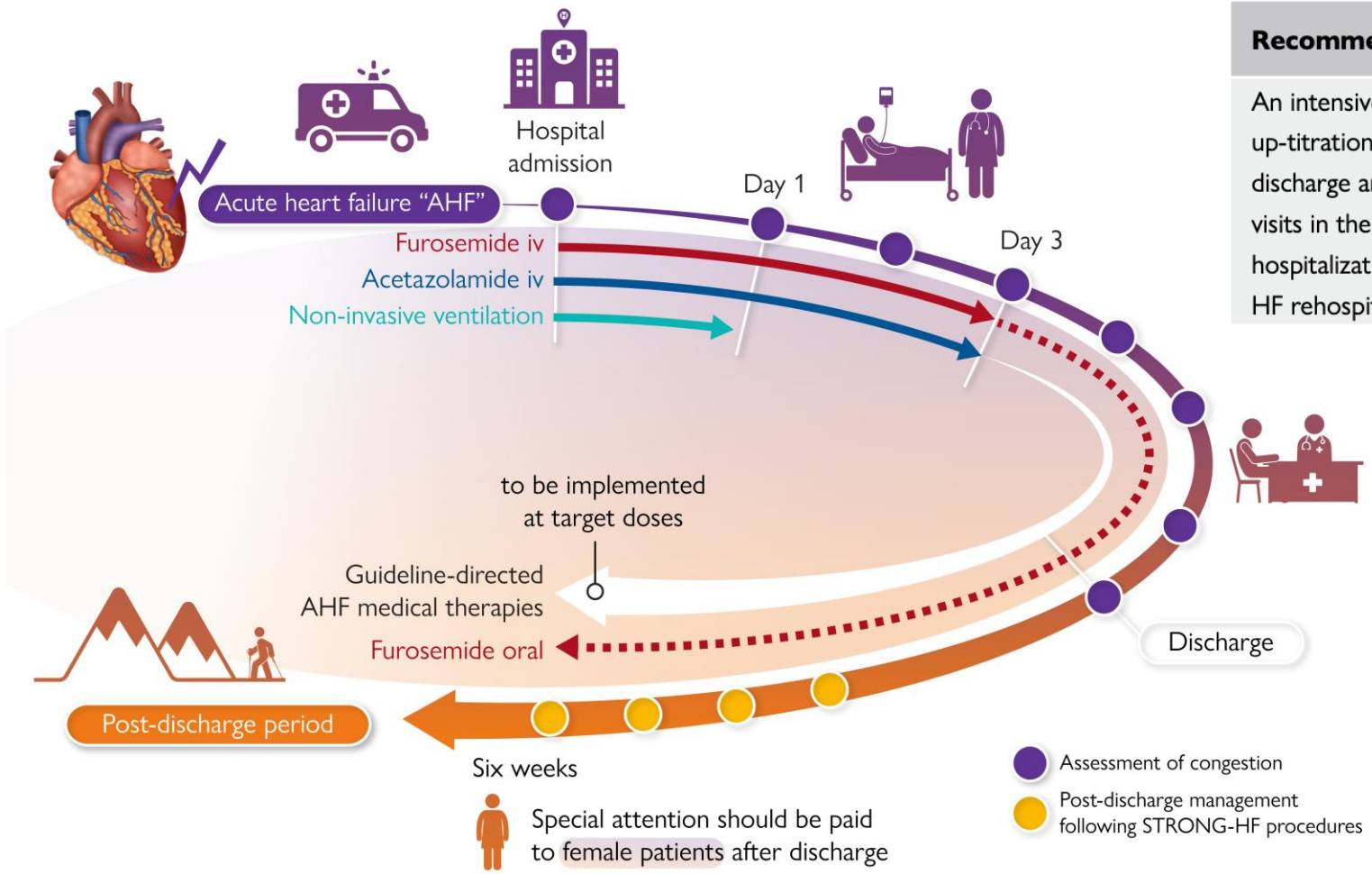
Tomasoni et al. JCF 2023

Route van een patiënt met AHF



Recommendation	Class[a]	Level[b]
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.[c,d,e] 16	I	B

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Deniau et al. EHJ 2023; McDonagh et al. EHJ 2023

Een intensieve stategie bij AHF

1. Start met adequate dosering lisdiureticum
    1. Op basis van thuisdosering en nierfunctie

2. Bepaal respons middels natriurese

3. Bij onvoldoende respons: optimaliseer lisdiuretica/start combinatie diuretica therapie
    Voor combinatietherapie acetazolamide eerste keus (ADVOR)

4. Vroege initiatie van GDMT tijdens hospitalisatie


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