Herzinsuffizienz Update

Georg Noll

Conflicts of Interest

Honorare für Vorträge/Consulting:

Amgen, Bayer, Novartis, MSD, Sanofi, Servier,
St. Jude, Vifor

Studien von/mit:

Amgen, Sanofi, Novartis

HERZKLINIK
HIRSLANDEN

Heart Clinic
Foundation

ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–13
https://doi.org/10.1093/eurheartj/ehad195

ESC GUIDELINES

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

McDonagh TA et al: Eur Heart J 2023

Epidemiologie der Herzinsuffizienz

Prävalenz

- >2-3% der Bevölkerung, 10 - 20% bei >70 Jahre alten
- Europa: >15 Millionen Patienten mit Herzinsuffizienz, Zahl steigend
- 20% Lebensrisiko für Herzinsuffizienz

Bedeutung

- 5% primärer Grund für Hospitalisation
- 10% der hospitalisierten Patienten
- 2% der Gesundheitskosten (60 - 70% wegen Hospitalisationen)
- 40% der wegen Herzinsuffizienz hospitalisierten Patienten versterben oder werden wieder hospitalisiert innerhalb eines Jahres
- Stark eingeschränkte Lebensqualität

McMurray JJ et al: Eur Heart J 33:1787; 2012
Dickstein K et al: Eur Heart J 29: 2388; 2006

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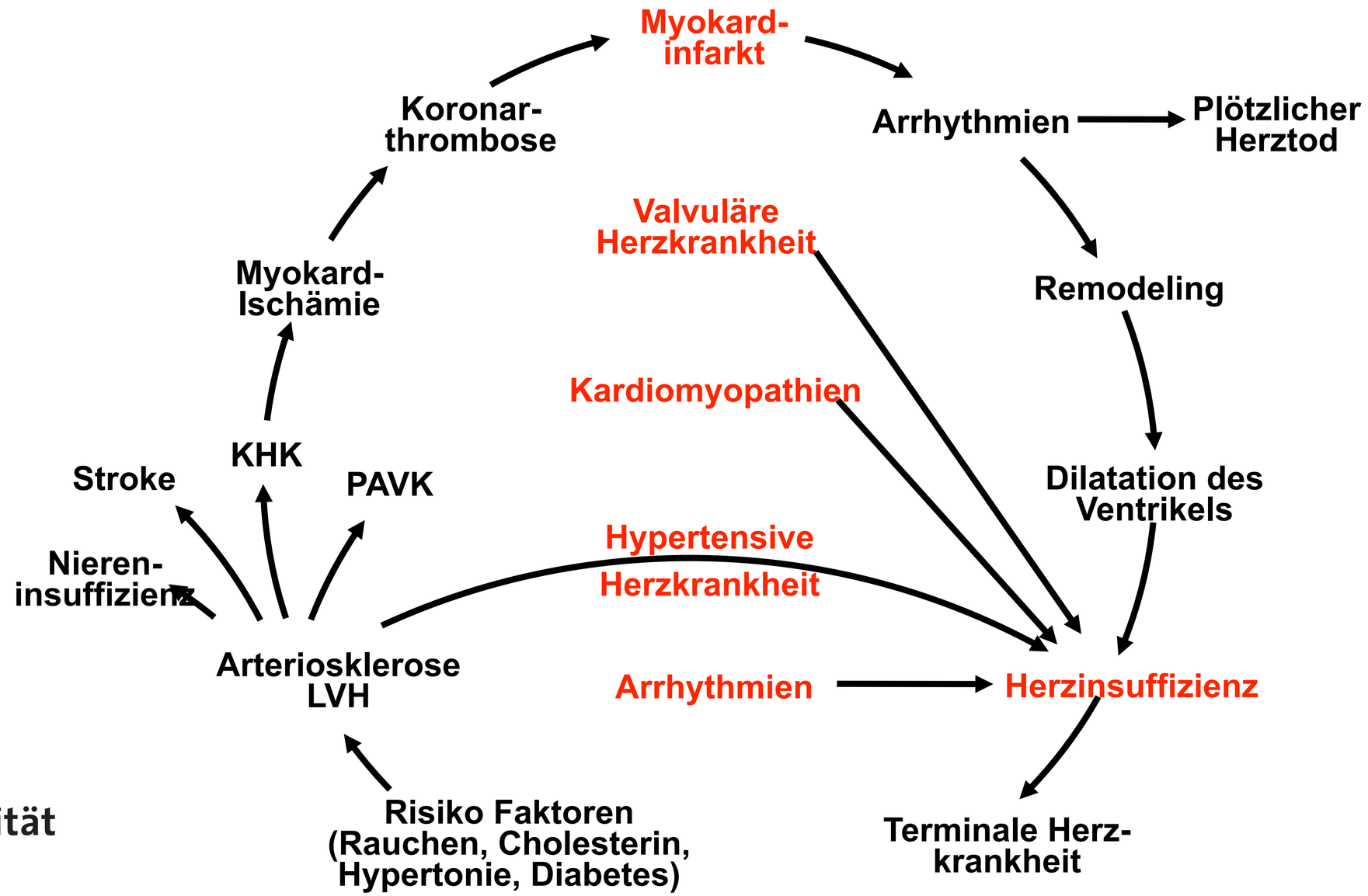
Ursachen der Herzinsuffizienz



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Definition of Different Forms of Heart Failure

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

McDonagh TA et al: Eur Heart J 2021

Seattle Heart Failure Risk Calc

By Epocrates

Open iTunes to buy and download apps.

View More by This Developer

Description

Seattle Heart Failure Risk Calc is based on the Seattle Heart Failure Model, which provides an accurate estimate of one-, two-, and five-year survival rates and average years of survival for patients with heart failure. The model incorporates medications and devices that are used to treat heart failure and how altering these affect survival.

Epocrates Web Site Seattle Heart Failure Risk Calc Support ...More

What's New in Version 1.2

Maintenance

View in iTunes

Free

Category: Medical
Updated: Feb 11, 2011
Version: 1.2
Size: 1.1 MB
Language: English
Seller: Epocrates

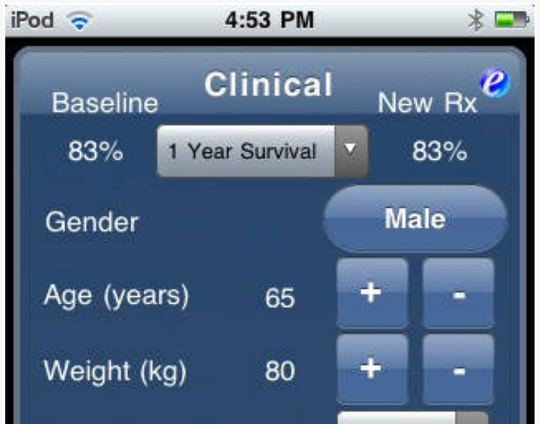
Rated 4+

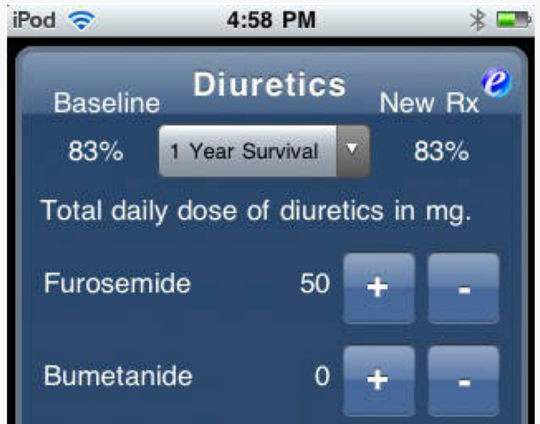
Compatibility: Requires iOS 3.0 or later. Compatible with iPhone, iPad, and iPod touch.

Customer Ratings

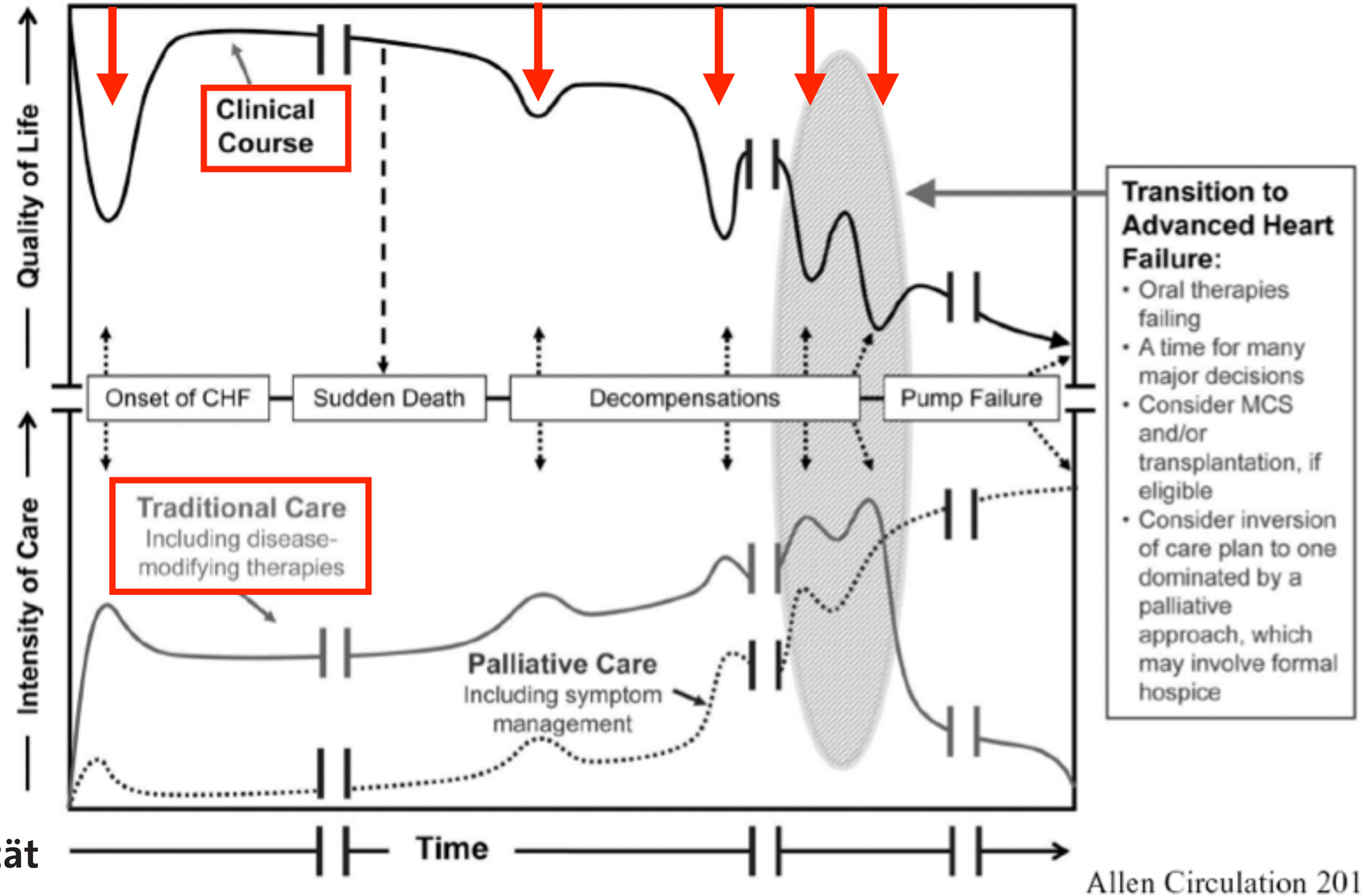
Current Version:
★★★½ 35 Ratings

iPhone Screenshot





Natural Course of Heart Failure



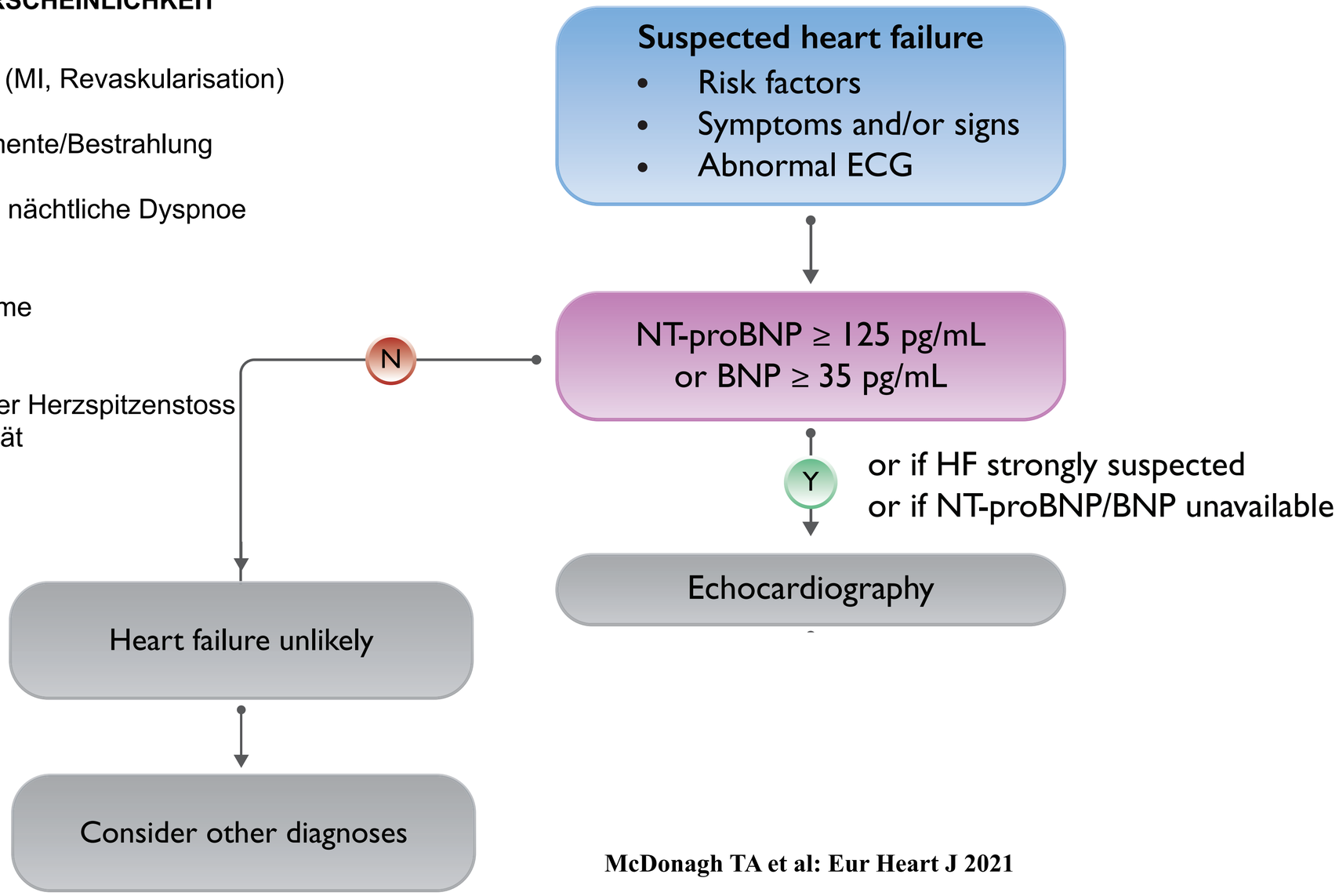
Allen Circulation 2012

Lanken Am J Respir Crit Care Med 2008

Diagnostischer Algorithmus für die Diagnose einer Herzinsuffizienz

BEURTEILUNG DER WAHRSCHEINLICHKEIT

1. **Anamnese**:
   Koronare Herzkrankheit (MI, Revaskularisation)
   Arterielle Hypertonie
   Kardiotoxische Medikamente/Bestrahlung
   Diuretikum-Behandlung
   Orthopnoe / paroxysmal nächtliche Dyspnoe
2. **Untersuchung**:
   Lungenstauung
   Beidseitige Knöchelödeme
   Herzgeräusch
   Halsvenenstauung
   Lateralisierter/verbreiteter Herzspitzenstoss
3. **EKG**: Jegliche Abnormität



McDonagh TA et al: Eur Heart J 2021

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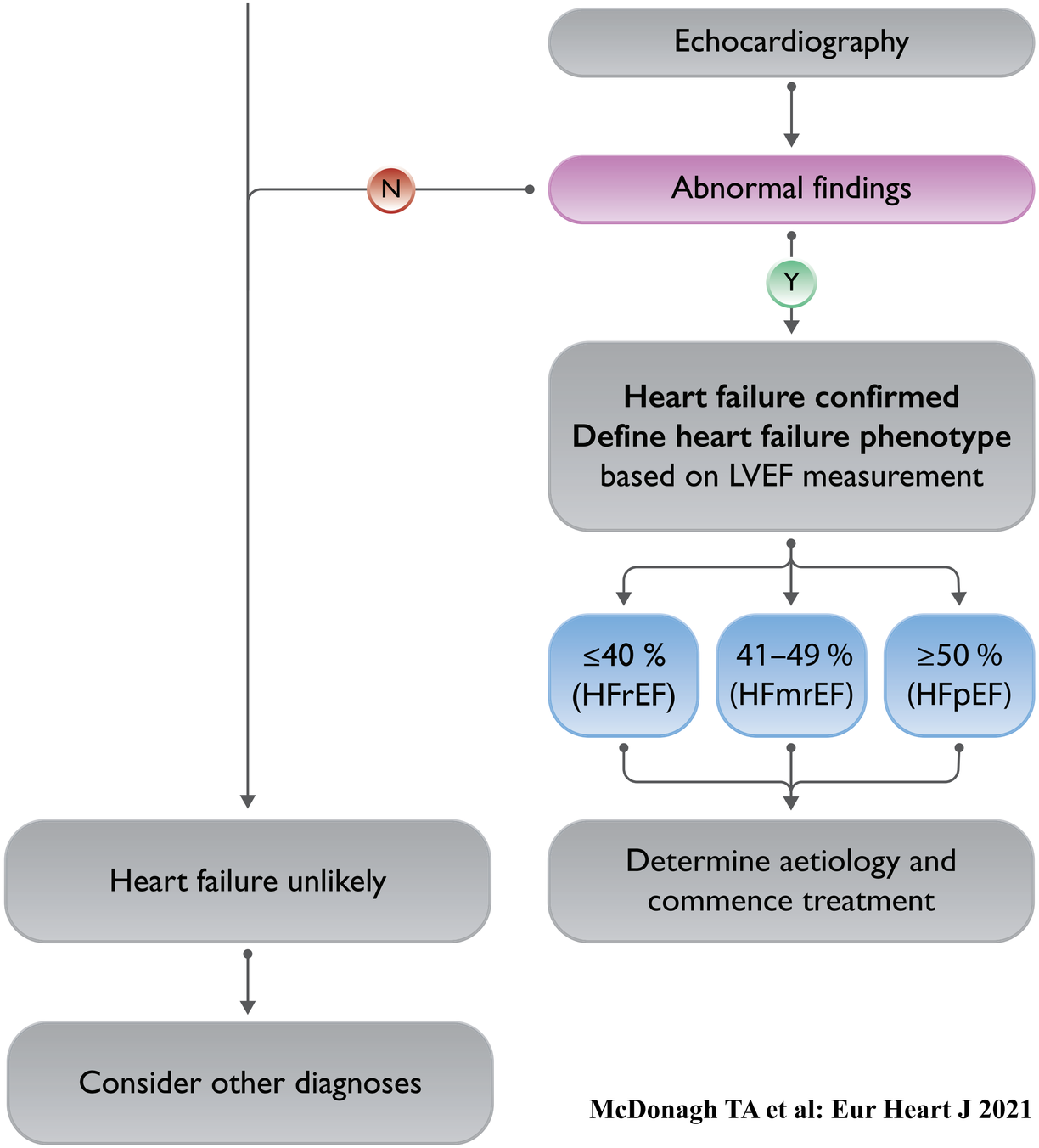


McDonagh TA et al: Eur Heart J 2021

(NT-pro)BNP bei Herzinsuffizienz

Hilfreich für

- Diagnose (Ausschluss)
- Schweregrad
- Prognose
- Therapiesteuerung?

Nicht-medikamentöse Massnahmen bei Herzinsuffizienz

1. Normalisierung des Körpergewichts
2. Salzrestriktion <5g/d (ESC, <3 g/d (WHO) ?
   KEINE SALZEXZESSE !
3. Kontrolle der Flüssigkeitszufuhr (1.5 - 2L/d, ESC)
   Bei Hyponatriämie !
4. Kontrolle der kardiovaskulären Risikofaktoren
5. Alkoholrestriktion (30g/d für Männer, 20 g/d für Frauen)
   Bei Alkohol-bedingter Kardiomyopathie: Absolute Alkoholkarenz
6. Regelmässige Bewegung
   Bei Dekompensation: Bettruhe

I‘ve made a diet and abstained
from fast food and alcohol –
in two weeks I lost 14 days.

Joe E. Lewis

comedian / singer in the 1920's

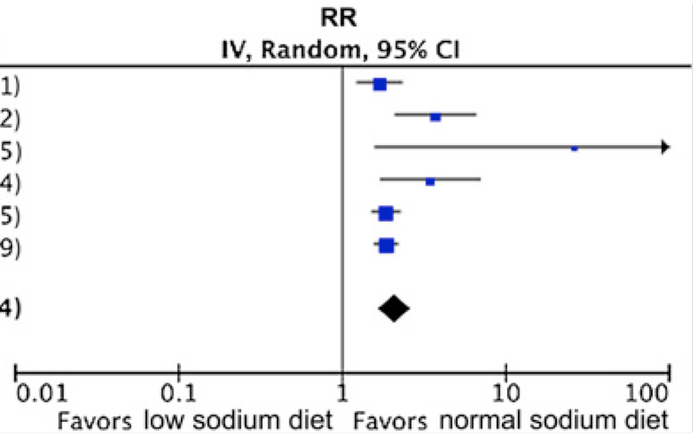
Low sodium versus normal sodium diets in systolic heart failure

Readmission for heart failure

Study or subgroup	Low sodium diet Events	Total	Normal sodium diet Events	Total	Weight	RR IV, Random, 95% CI
Licata *et al*, 2003[9]	43	54	25	53	21.3%	1.69 (1.23 to 2.31)
Parrinello *et al*, 2009[7]	44	86	12	87	11.2%	3.71 (2.11 to 6.52)
Paterna *et al*, 2005[10]	12	46	0	48	0.7%	26.06 (1.59 to 427.85)
Paterna *et al*, 2008[13]	30	114	9	118	8.2%	3.45 (1.72 to 6.94)
Paterna *et al*, 2009[11]	130	179	75	191	28.3%	1.85 (1.52 to 2.25)
Paterna *et al*, 2011[12]	305	890	163	881	30.3%	1.85 (1.57 to 2.19)
Total (95% CI)		**1369**		**1378**	**100.0%**	**2.10 (1.67 to 2.64)**
Total events	564		284			

Heterogeneity: $\tau^2=0.04$; $\chi^2=12.22$, df=5 (p=0.03); $I^2=59\%$

Test for overall effect: Z=6.39 (p<0.00001)

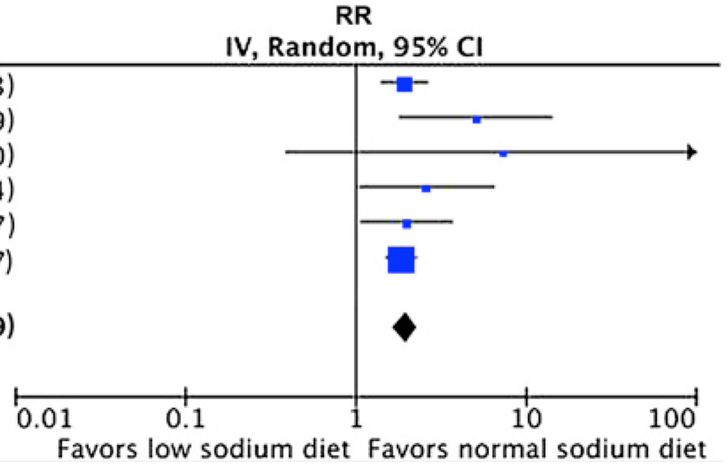


Mortality

Study or subgroup	Low sodium Events	Total	Normal sodium Events	Total	Weight	RR IV, Random, 95% CI
Licata *et al*, 2003[9]	47	54	24	53	26.6%	1.92 (1.41 to 2.63)
Parrinello *et al*, 2009[7]	20	86	4	87	2.5%	5.06 (1.80 to 14.19)
Paterna *et al*, 2005[10]	3	46	0	48	0.3%	7.30 (0.39 to 137.50)
Paterna *et al*, 2008[13]	15	114	6	118	3.1%	2.59 (1.04 to 6.44)
Paterna *et al*, 2009[11]	26	179	14	191	6.9%	1.98 (1.07 to 3.67)
Paterna *et al*, 2011[12]	212	890	114	881	60.6%	1.84 (1.50 to 2.27)
Total (95% CI)		**1369**		**1378**	**100.0%**	**1.95 (1.66 to 2.29)**
Total events	323		162			

Heterogeneity: $\tau^2=0.00$; $\chi^2=4.73$, df=5 (p=0.45); $I^2=0\%$

Test for overall effect: Z=8.08 (p<0.00001)



FRESH-UP

nature medicine

Article

https://doi.org/10.1038/s41591-025-03628-4

Liberal fluid intake versus fluid restriction in chronic heart failure: a randomized clinical trial

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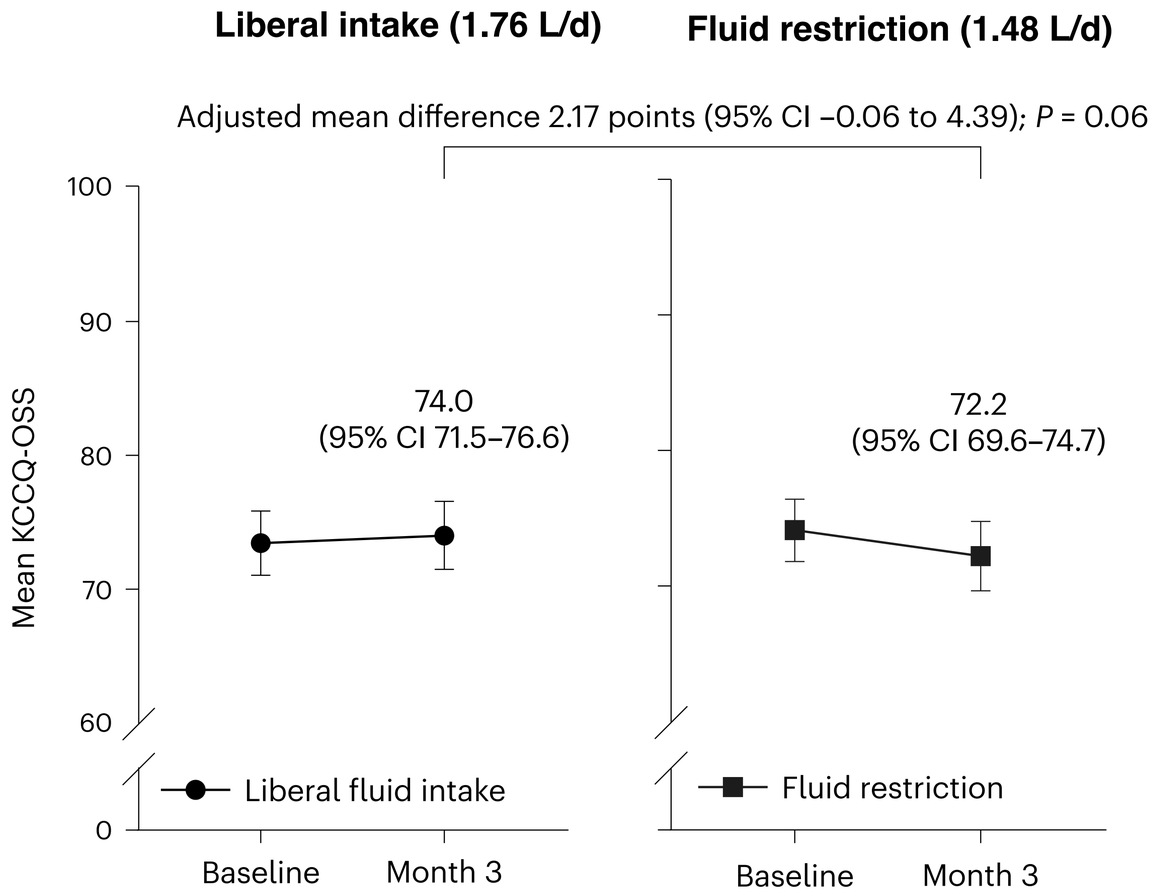
Published online: 30 March 2025

Check for updates

Job J. Herrmann[1,2], Hans-Peter Brunner-La Rocca[3,4], Lisette E. H. J. M. Baltussen[1], Fabienne Beckers-Wesche[3], Sebastiaan C. A. M. Bekkers[5], Louise Bellersen[1], J. W. Martijn van Eck[6], H. Carlijne Hassing[1], Tiny Jaarsma[7,8], Gerard C. M. Linssen[9], Ron Pisters[10], Sandra Sanders-van Wijk[11], Marjolein H. I. Verdijk[1], M. Louis Handoko[8], Peter van der Meer[12], Frederik H. Verbrugge[13,14], James L. Januzzi Jr[15], Antoni Bayés-Genís[16], Robby Nieuwlaat[17], Laura Rodwell[18], D. H. Frank Gommans[1,19] & Roland R. J. van Kimmenade[1]

FRESH-UP

	Liberal fluid intake (*n*=254)	Fluid restriction (*n*=250)
Age, years	69.4±10.6	69.0±10.8
Male	170 (66.9)	169 (67.6)
White[a]	247 (97.2)	245 (98.0)
Quality of life		
KCCQ-OSS	76.0 [59.9–90.2]	77.7 [61.7–88.5]
TDS-HF	15.0 [10.0–22.0]	16.0 [11.0–21.0]
EQ-5D-5L	0.85 [0.71–0.92]	0.81 [0.70–0.91]
NYHA functional class		
II	218 (85.8)	221 (88.4)
III	36 (14.2)	29 (11.6)
LVEF		
%	40.3±10.9	40.2±10.8
HFrEF	136 (53.5)	124 (49.6)
HFmrEF	60 (23.6)	70 (28.0)
HFpEF	58 (22.8)	56 (22.4)
Cause of HF		
Ischemic	108 (42.5)	113 (45.2)
Nonischemic	146 (57.5)	137 (54.8)
HF duration, years	5.0 [2.0–10.0]	4.0 [2.0–10.0]



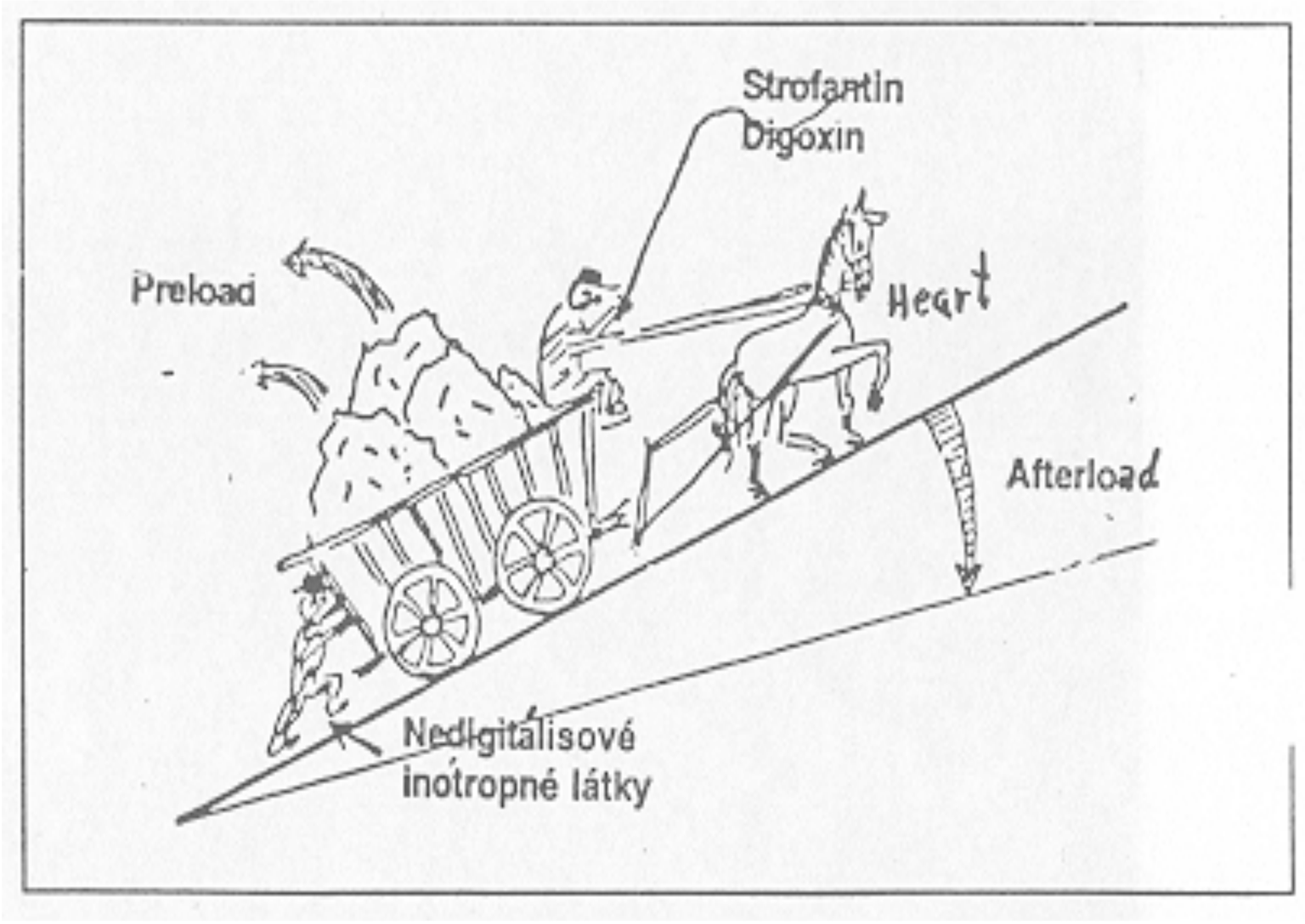
Key secondary outcome (Thirst distress scale)			
TDS-HF	16.9 (15.8–18.0)	18.6 (17.5–19.6)	<0.001[a]

Herrmann JJ et al: Nature Med 2025

Nicht-medikamentöse Massnahmen bei Herzinsuffizienz

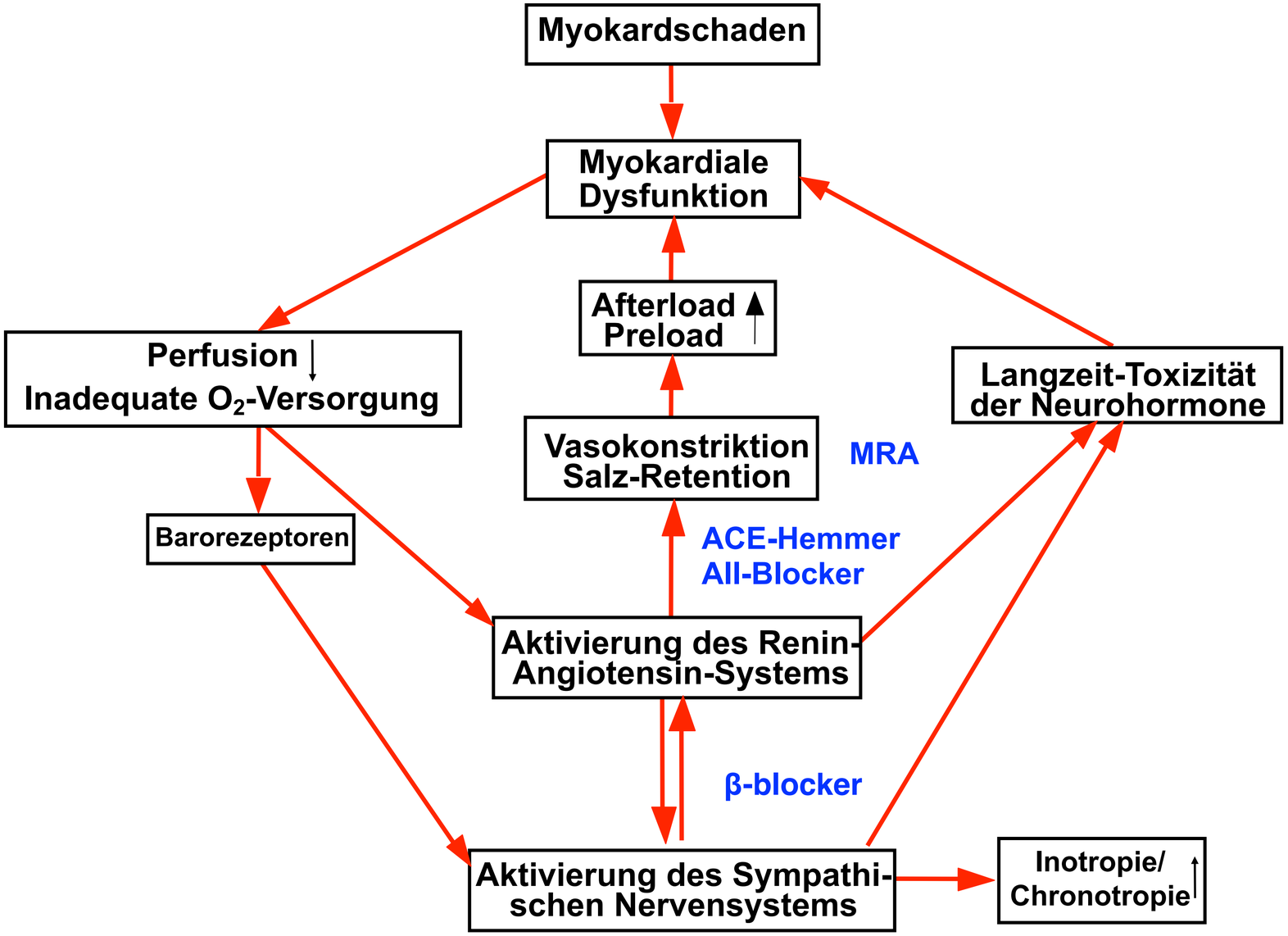
1. Normalisierung des Körpergewichts
2. Salzrestriktion <5g/d (ESC, <3 g/d (WHO) ?
   KEINE SALZEXZESSE !
3. Kontrolle der Flüssigkeitszufuhr (1.5 - 2L/d, ESC)
   Bei Hyponatriämie !
4. Kontrolle der kardiovaskulären Risikofaktoren
5. Alkoholrestriktion (30g/d für Männer, 20 g/d für Frauen)
   Bei Alkohol-bedingter Kardiomyopathie: Absolute Alkoholkarenz
6. Regelmässige Bewegung
   Bei Dekompensation: Bettruhe

Therapie-Prinzipien bei Herzinsuffizienz

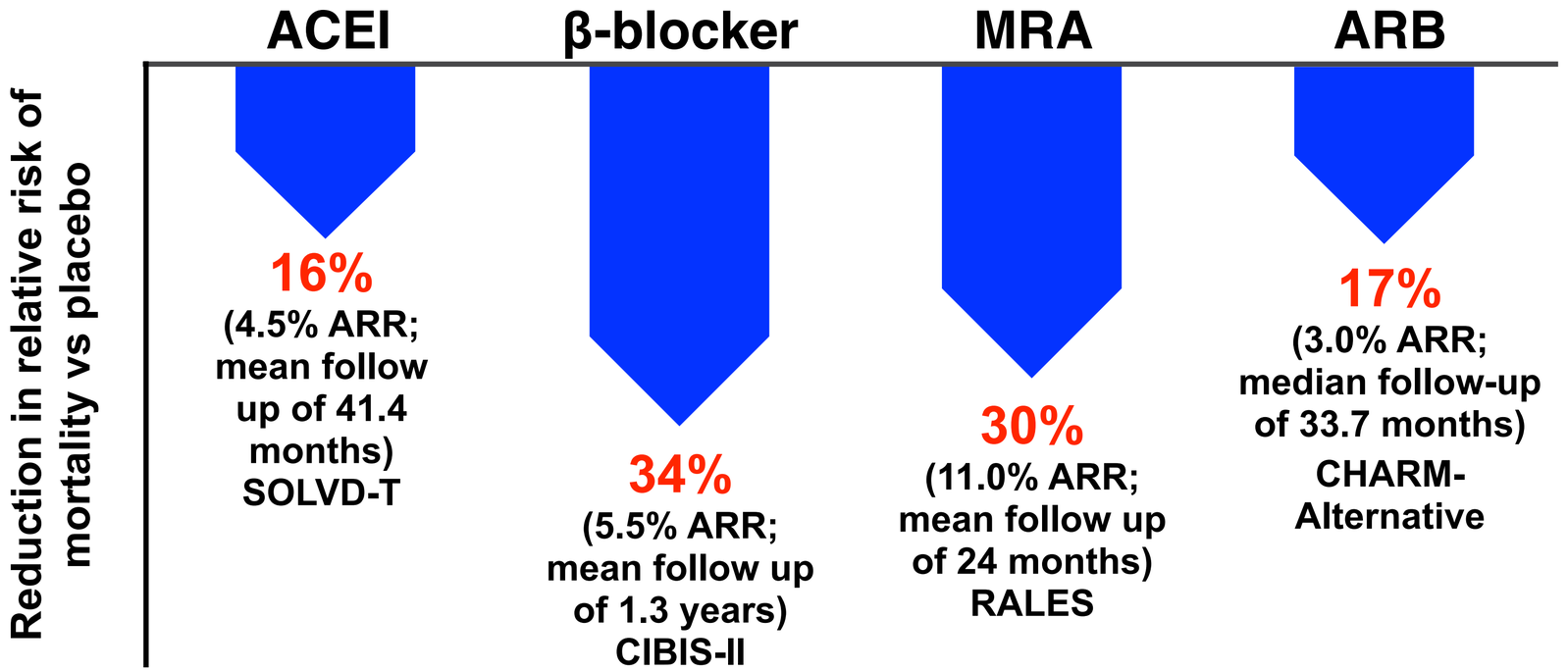


Courtesy of Otto Hess

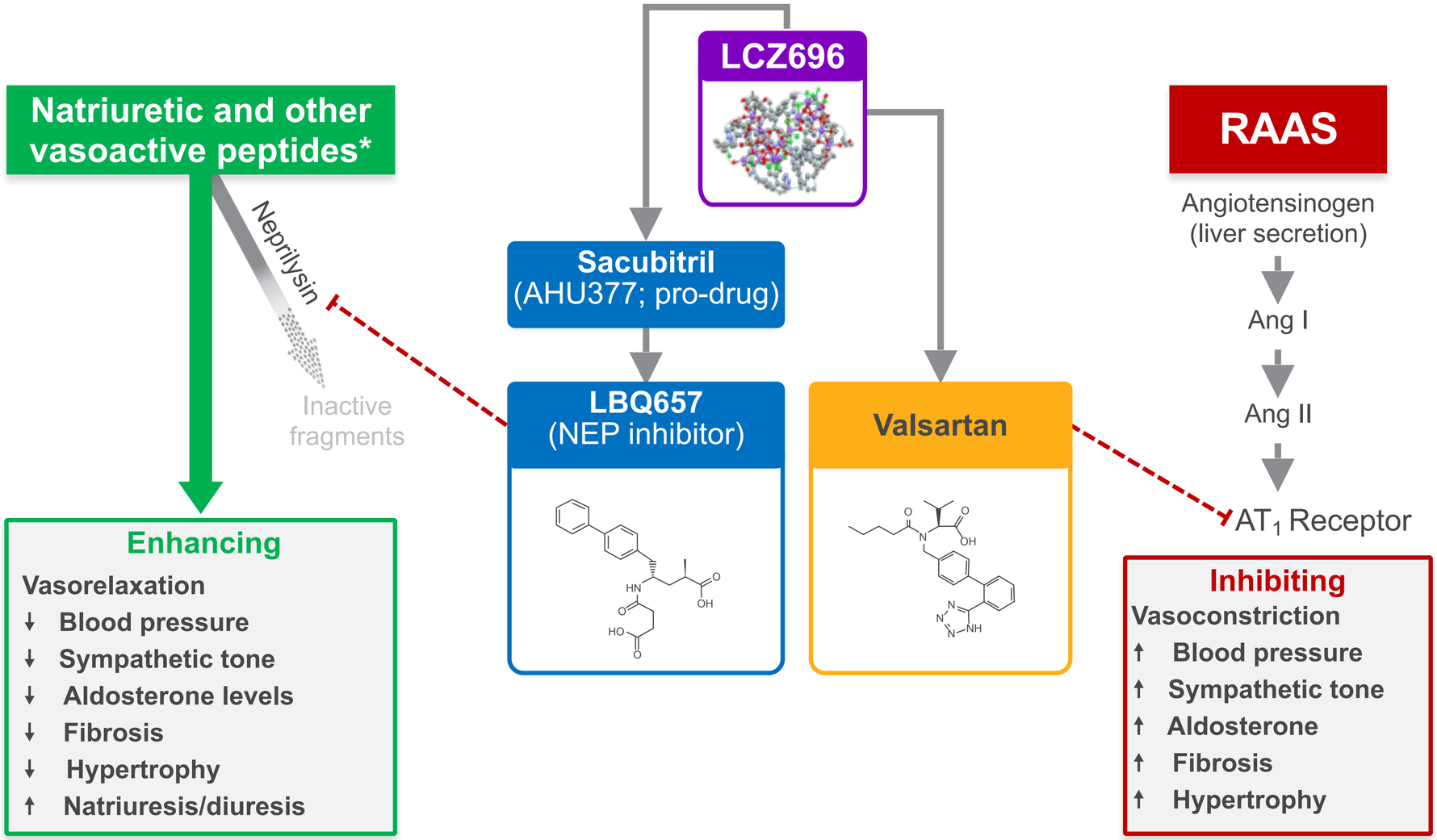
Neurohumorale Mechanismen der Herzinsuffizienz



Effects of neurohumoral Inhibitors on Survival in Heart Failure with Reduced Ejection Fraction



Mode of Action of LCZ696 (Entresto): It simultaneously inhibits NEP (via LBQ657) and blocks the AT_1 receptor (via valsartan)



***Neprilysin substrates listed in order of relative affinity for NEP: ANP, CNP, Ang II, Ang I, adrenomedullin, substance P, bradykinin, endothelin-1, BNP**

Levin et al. N Engl J Med 1998;339:321–8; Nathisuwan & Talbert. Pharmacotherapy 2002;22:27–42;
Schrier & Abraham N Engl J Med 2009;341:577–85; Langenickel & Dole. Drug Discov Today: Ther Strateg 2012;9:e131–9;
Feng et al. Tetrahedron Letters 2012;53:275–6

The NEW ENGLAND JOURNAL of MEDICINE

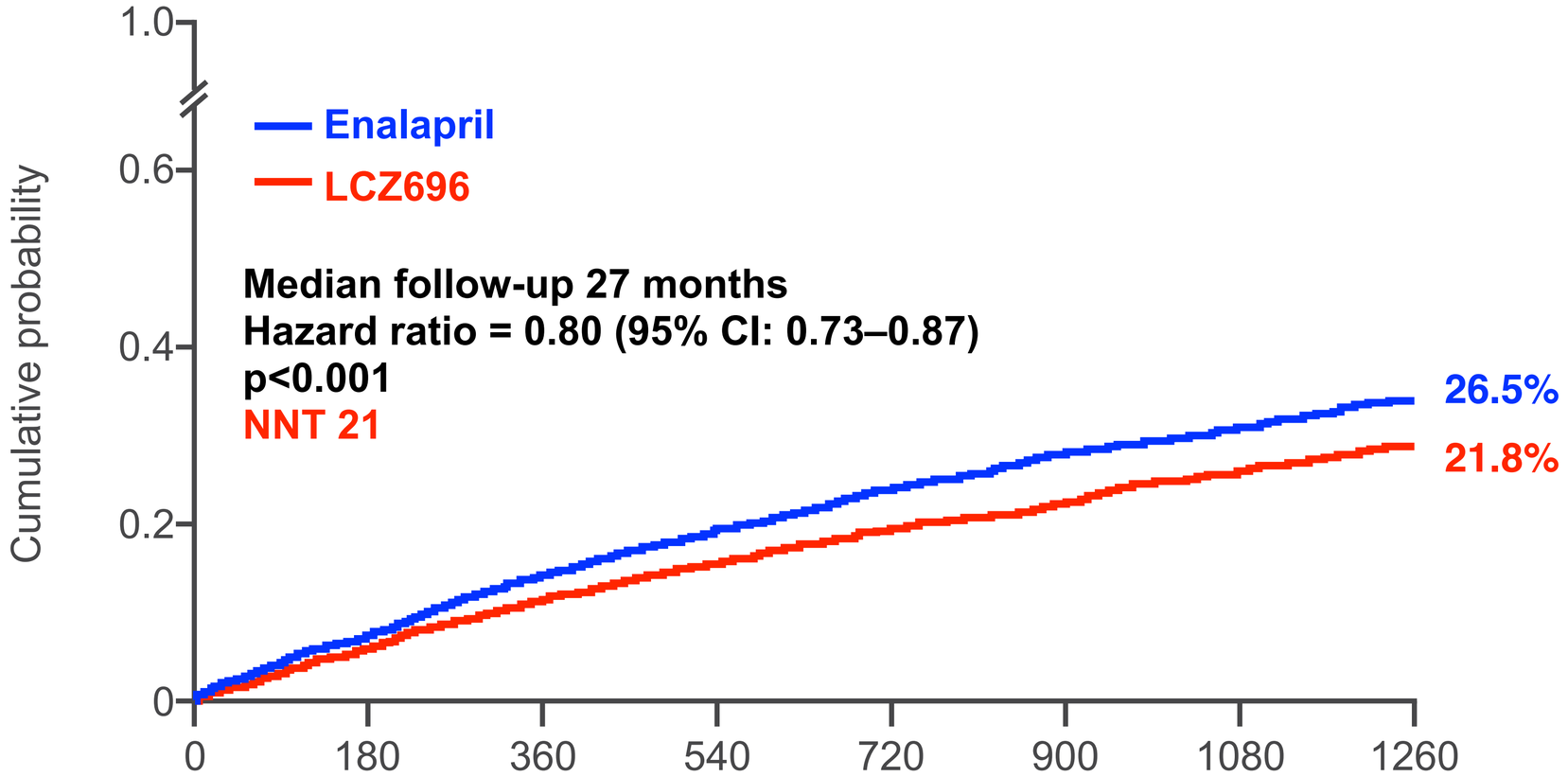
ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

McMurray JJ. *et al.* N Engl J Med. 2014;371(11):993-1‘004.

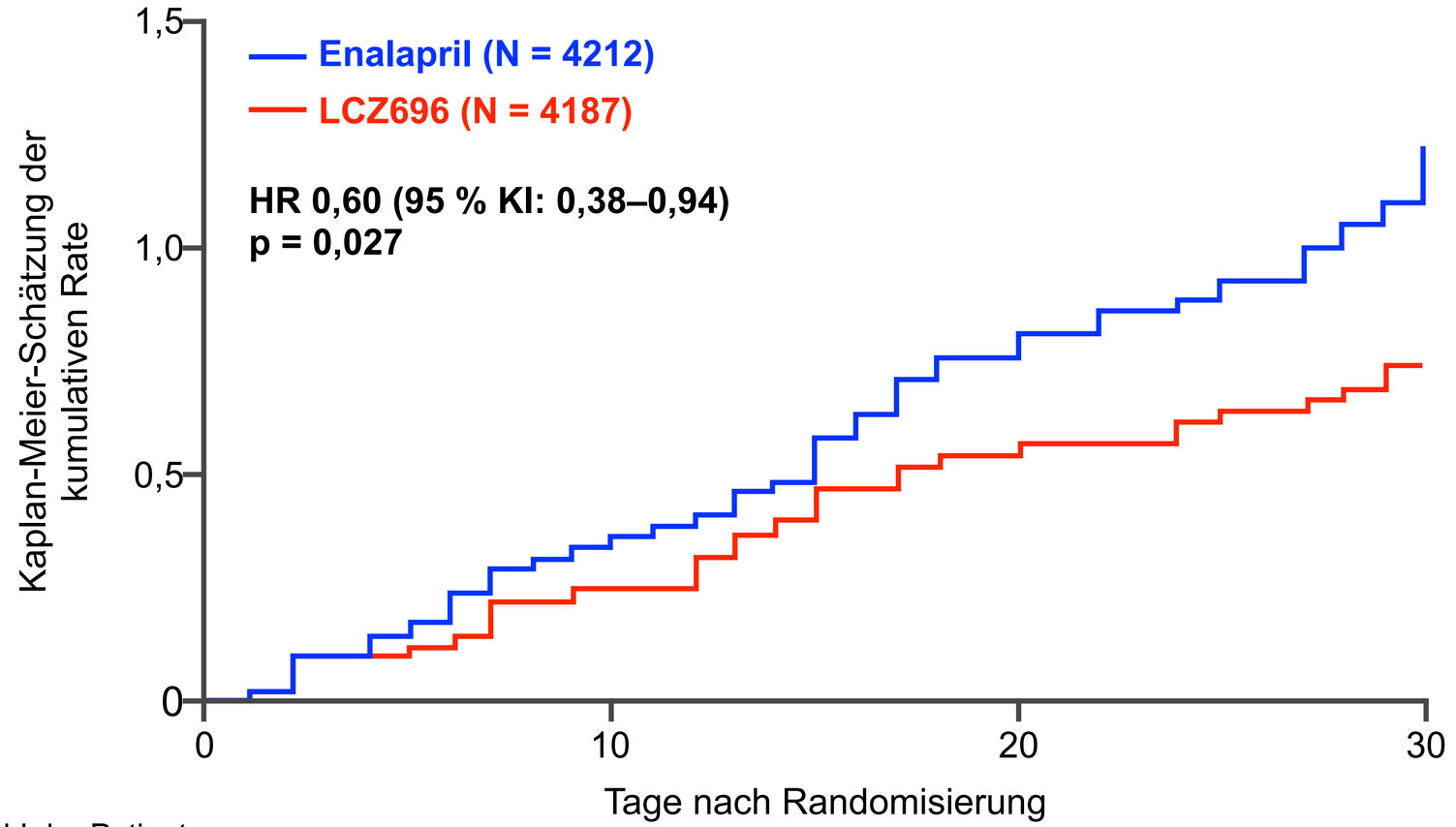
PARADIGM-HF: Primary endpoint: Death from CV causes or first hospitalization for HF



No at risk								
LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

McMurray JJ. *et al.* N Engl J Med. 2014;371(11):993-1‘004.

PARADIGM-HF
Primary Endpoint at day 30



Anzahl der Patienten				
LCZ696	4187	4174	4153	4140
Enalapril	4212	4192	4166	4143

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Packer M, *et al*. Circulation. 2015 Jan 6;131(1):54-61.

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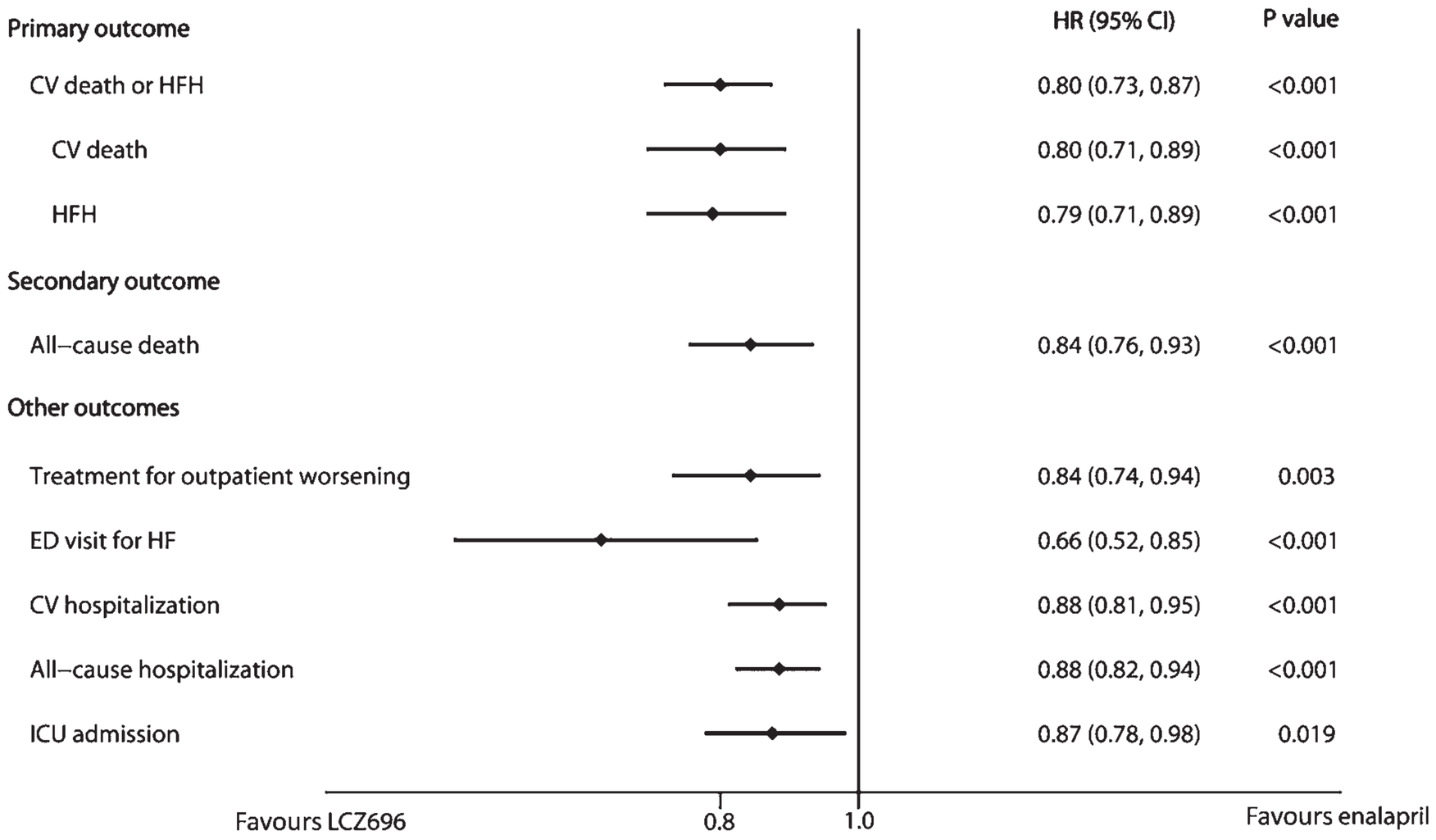
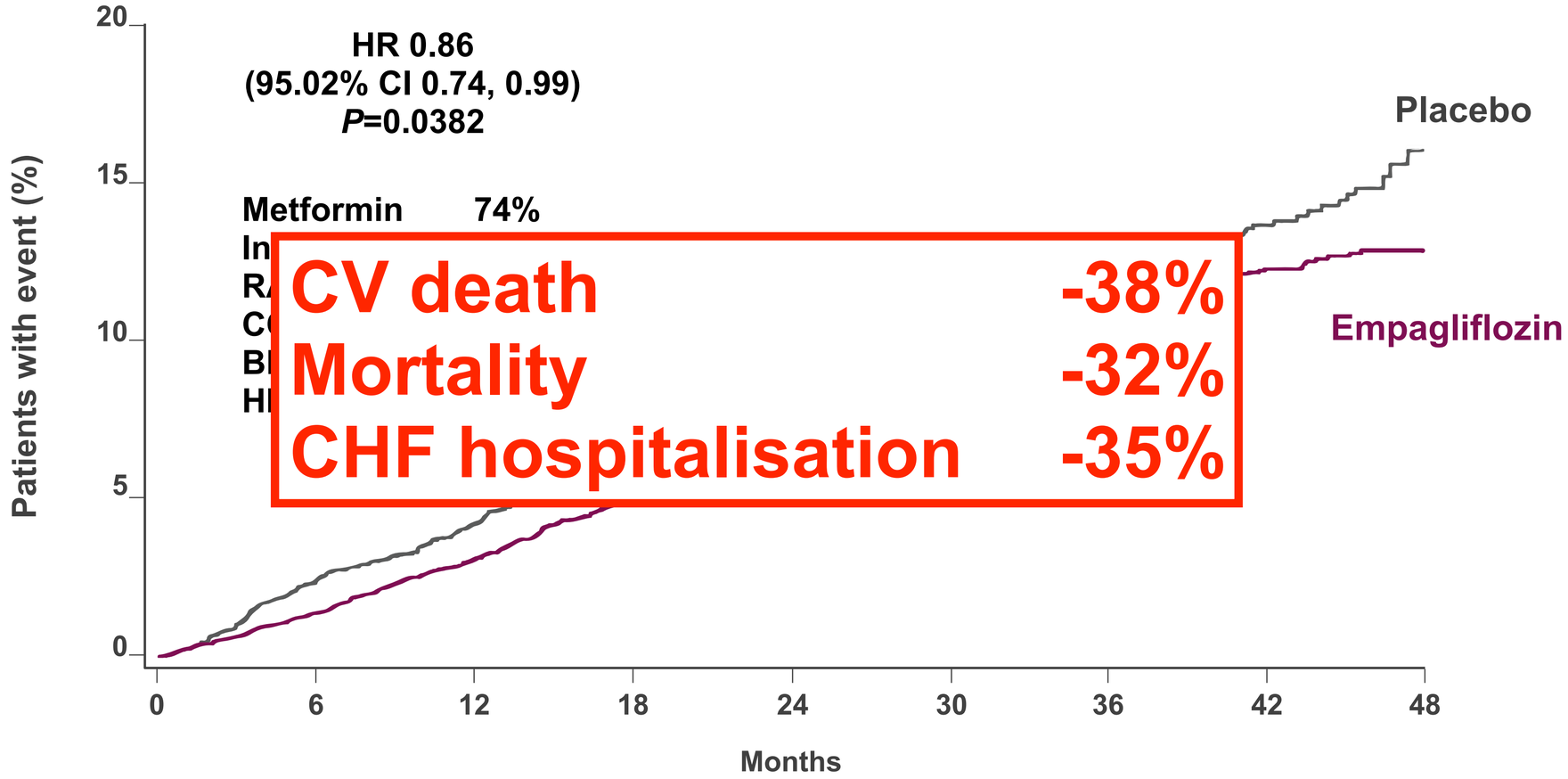
Other Outcomes in PARADIGM-HF



McMurray JJV: Eur Heart J 2015

EMPA-REG: Primary Endpoint (CV death, nonfatal MI, nonfatal stroke)



No. of patients									
Empagliflozin	4687	4580	4455	4328	3851	2821	2359	1534	
Placebo	2333	2256	2194	2112	1875	1380	1161	741	166

Universität Zürich[UZH]

Zinman B, et al. N Engl J Med. 2015

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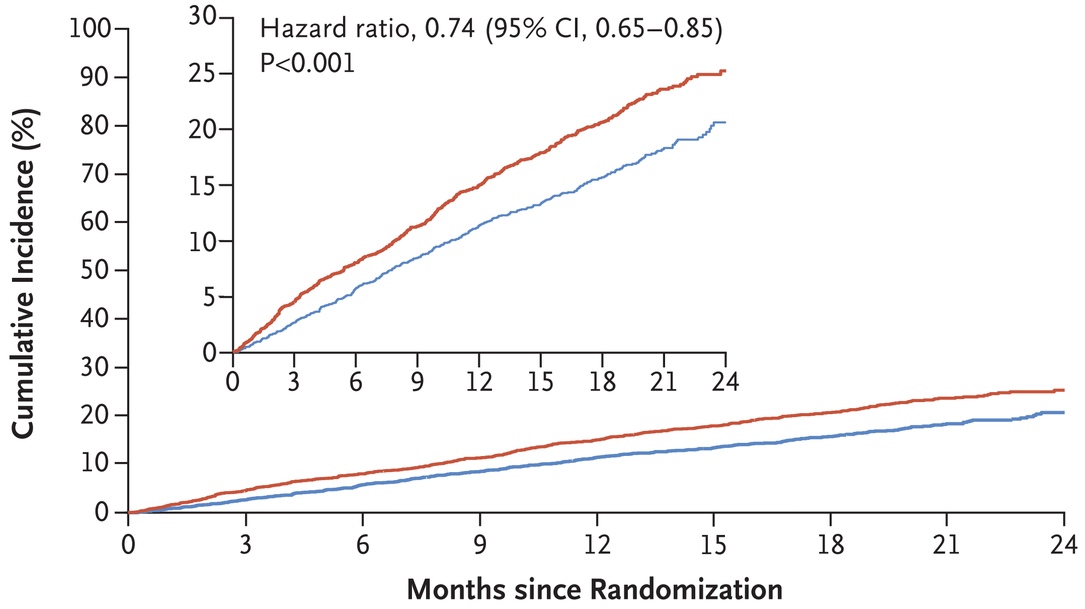
SGLT2-Hemmer bei Herzinsuffizienz

Kardiovaskulärer Tod oder Hospitalisation wegen Herzinsuffizienz

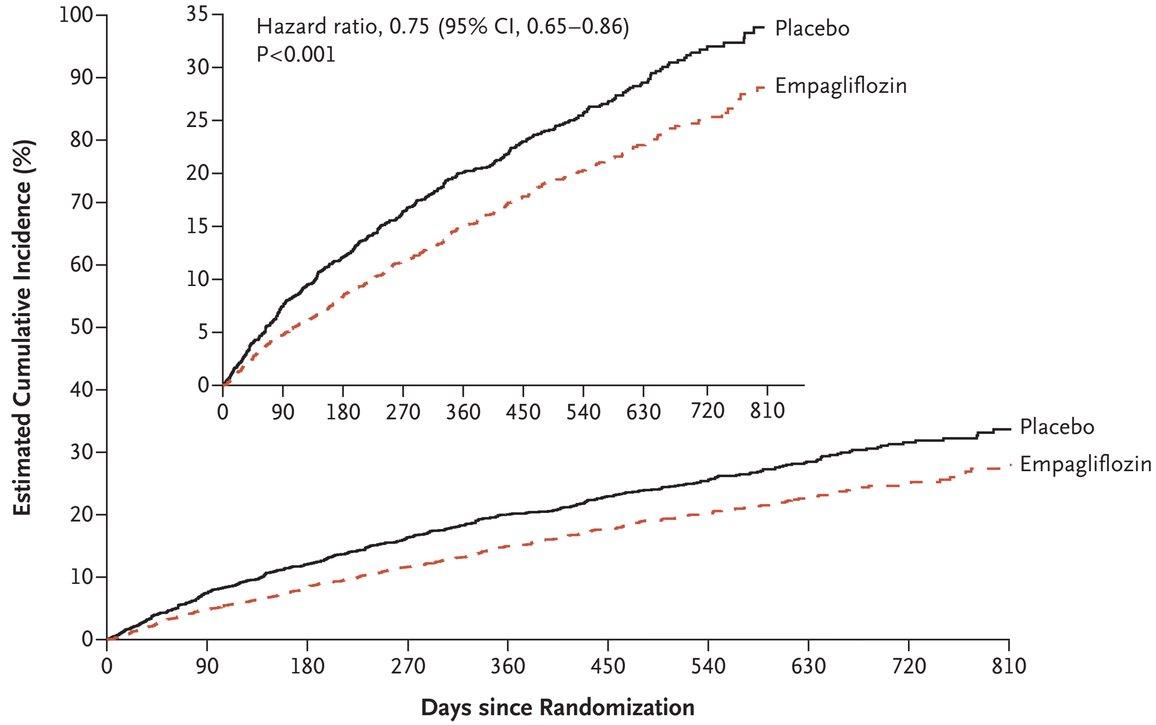
DAPA-HF



No. at Risk									
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210
Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210

McMurray JJV et al: NEJM 2019

EMPEROR-Reduced



No. at Risk										
Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

Packer M et al: NEJM 2020

SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials

Lancet 30.08.2020

Faiez Zannad, João Pedro Ferreira, Stuart J Pocock, Stefan D Anker, Javed Butler, Gerasimos Filippatos, Martina Brueckmann, Anne Pernille Ofstad, Egon Pfarr, Waheed Jamal, Milton Packer

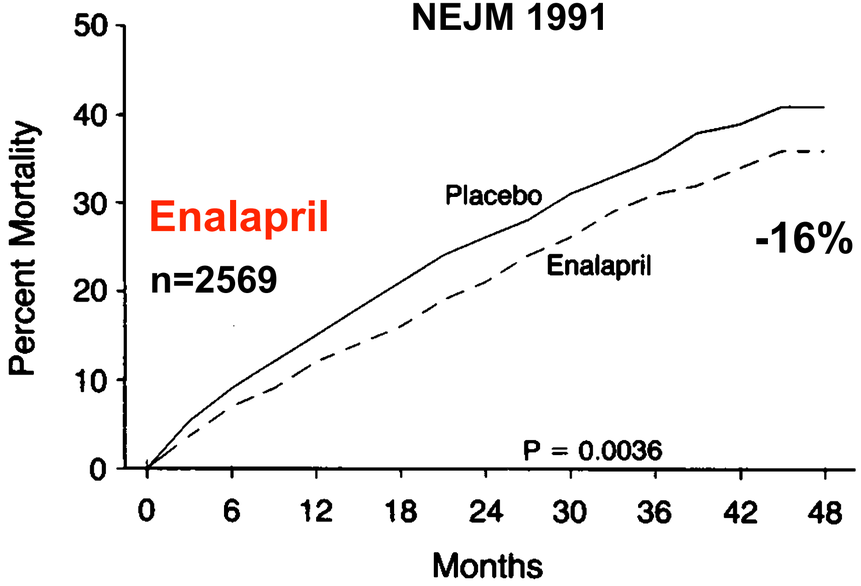
All-cause mortality	-13%
Cardiovascular death	-14%
Hosp for HF/cv death	-26%
Hosp for HF	-31%

Findings Among 8474 patie effect was a 13% reduction in all-cause death (pooled HR 0 n in cardiovascular death (0·86, 0·76–0·98; p=0·027). SGL duction in the combined risk of cardiovascular death or firs ·0001), and by a 25% decrease in the composite of recurrent H (0·75, 0·68–0·84; p<0·0001). The risk of the composite renal e All tests for heterogeneity of effect size between trials were not stent benefits for subgroups based on age, sex, diabetes, treatment with an ARNI and baseline eGFR, but suggested treatment-by-subgroup interactions for subgroups based on NYHA functional class and race.

Interpretation The effects of empagliflozin and dapagliflozin on hospitalisations for heart failure were consistent in the two independent trials and suggest that these agents also improve renal outcomes and reduce all-cause and cardiovascular death in patients with HFrEF.

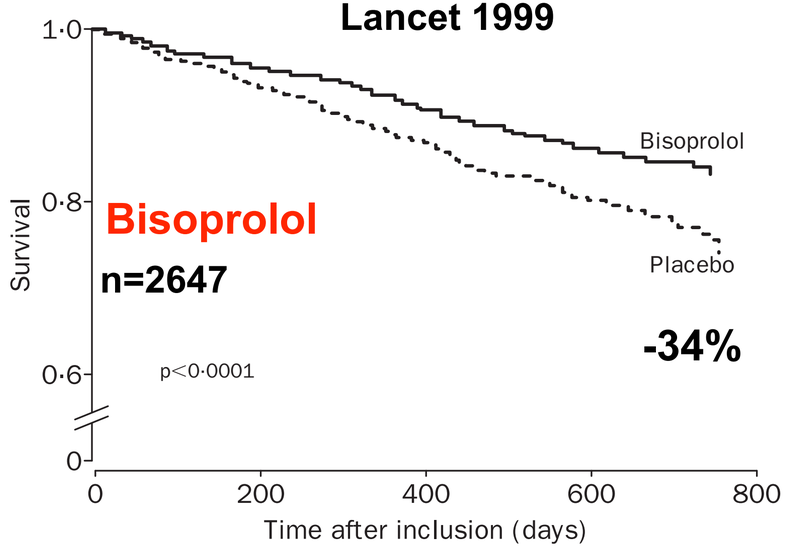
Mortalität in Landmark-Studien bei chronischer Herzinsuffizienz

SOLVD
NEJM 1991



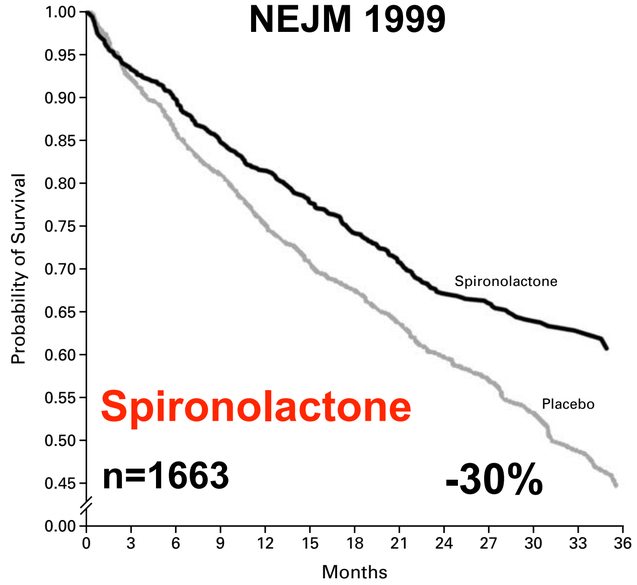
Enalapril
n=2569
-16%

CIBIS II
Lancet 1999



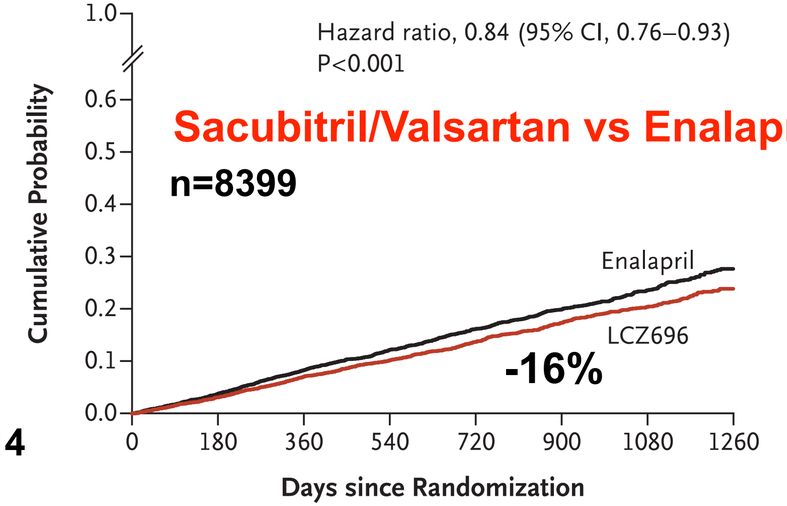
Bisoprolol
n=2647
-34%

RALES
NEJM 1999



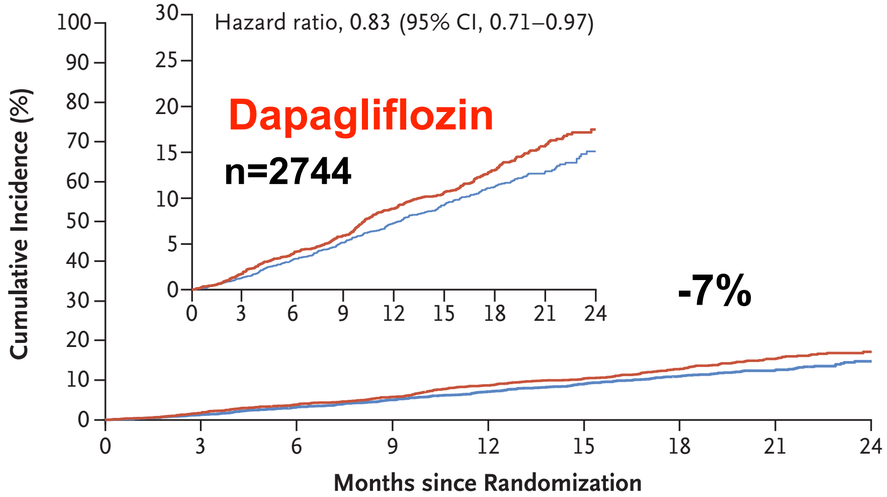
Spironolactone
n=1663
-30%

PARADIGM-HF
NEJM 2014



Sacubitril/Valsartan vs Enalapril
n=8399
-16%

DAPA-HF
NEJM 2021



Dapagliflozin
n=2744
-7%

Therapie der HFrEF

HERZKLINIK
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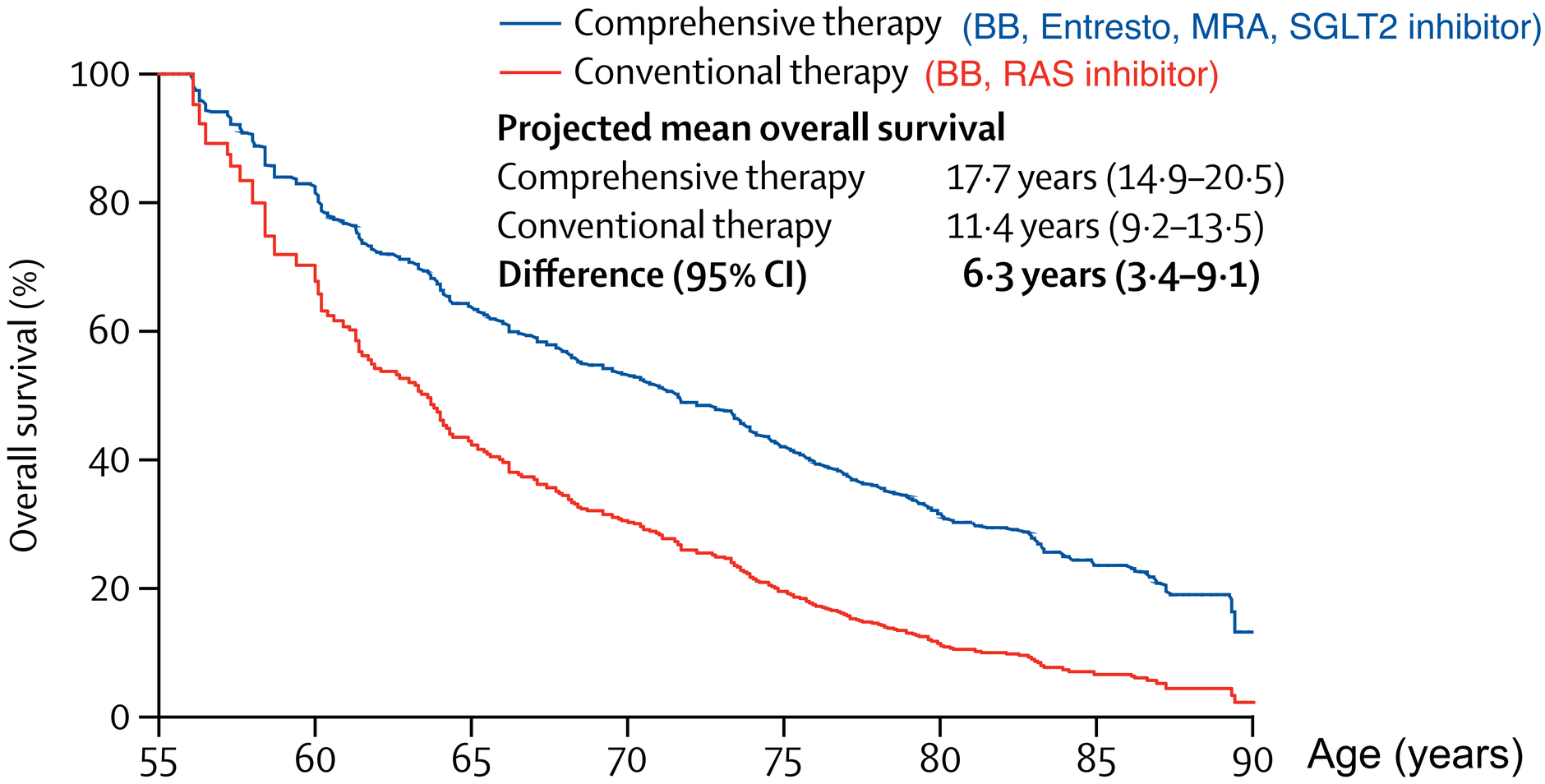
Projected mean survival of a 55 year old patient with heart failure and reduced ejection fraction

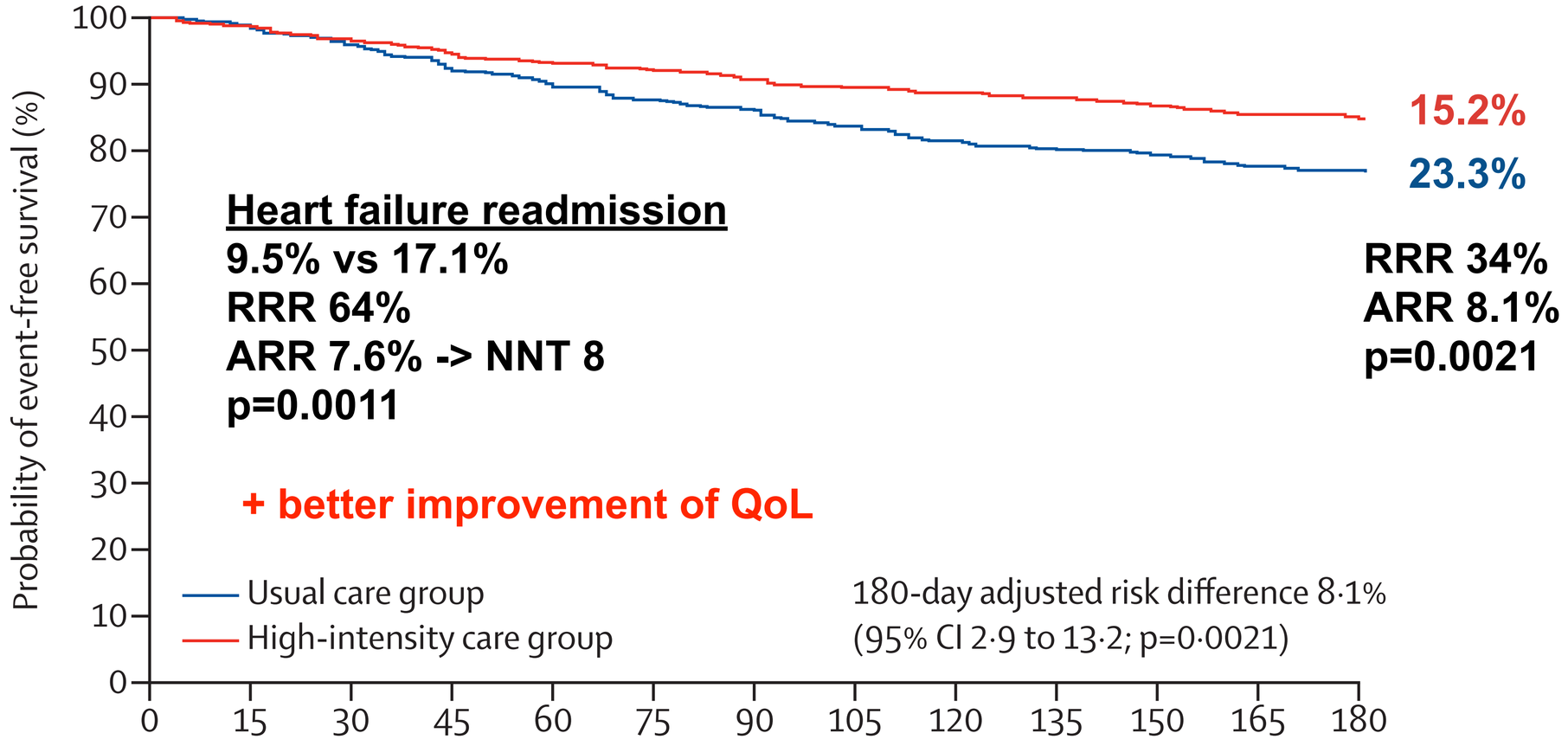


Vaduganathan M et al: Lancet 2020

Start l ? o slow

Strong-HF: All Cause Mortality, HF Hospitalisations

Visits at week 1, 2, 3, 6, 12, 25 after hospitalisation



Heart failure readmission
9.5% vs 17.1%
RRR 64%
ARR 7.6% -> NNT 8
p=0.0011

RRR 34%
ARR 8.1%
p=0.0021

+ better improvement of QoL

Number at risk

Usual care group	502	494	474	454	439	423	410	394	381	373	366	353	329
High-intensity care group	506	497	484	466	449	440	430	419	415	408	397	384	345

Mebazaa A et al: Lancet 2022

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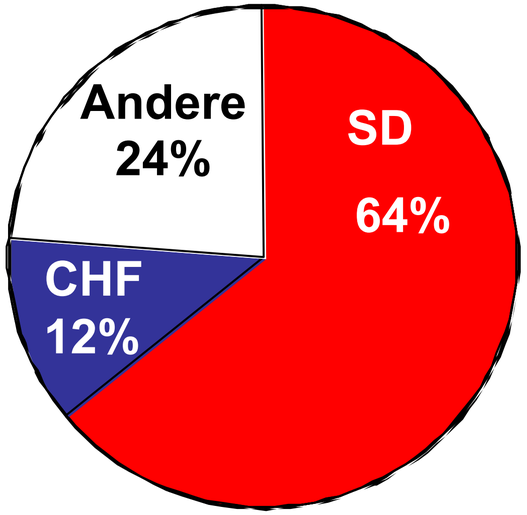
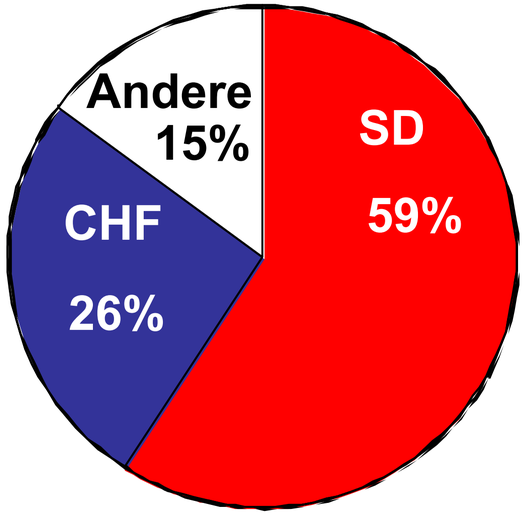
Todesursache nach NYHA Klasse in MERIT

NYHA II



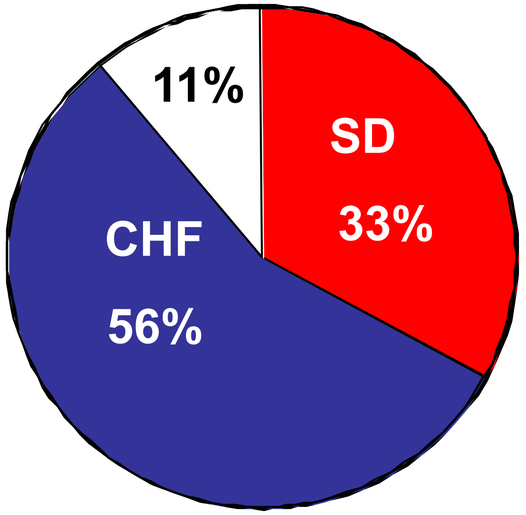
Anzahl Todesfälle
n=103

NYHA III



Anzahl Todesfälle
n=232

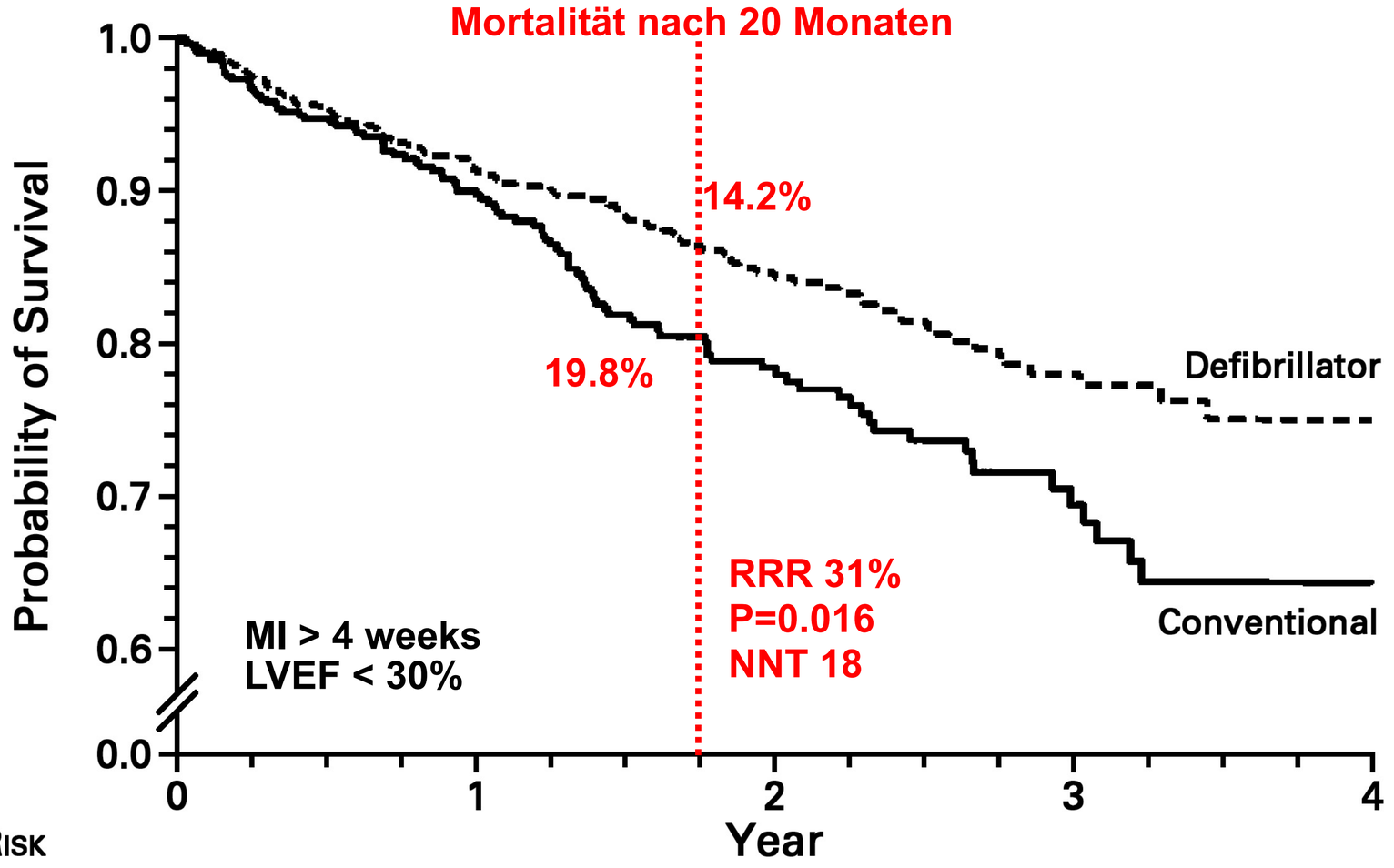
NYHA IV



Anzahl Todesfälle
n=27

CHF=Herzinsuffizienz
SD=plötzlicher Herztod

Einfluss eines internen Defibrillators auf das Überleben von Patients mit eingeschränkter linksventrikulärer Funktion nach Myokardinfarkt

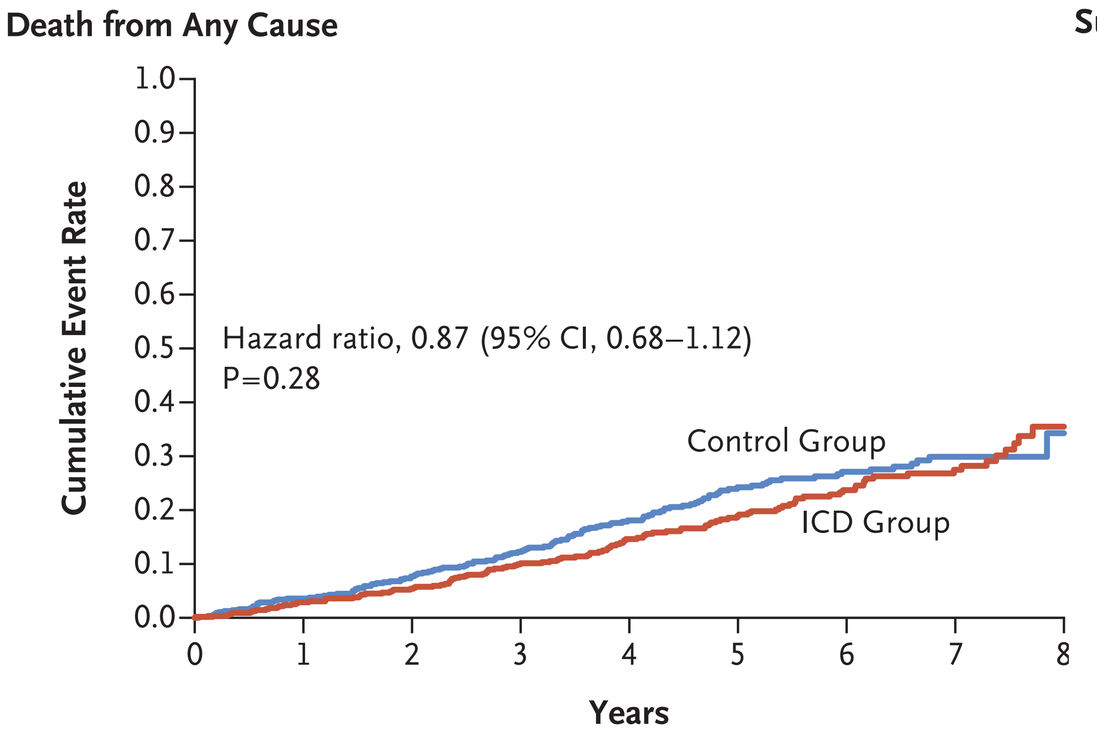


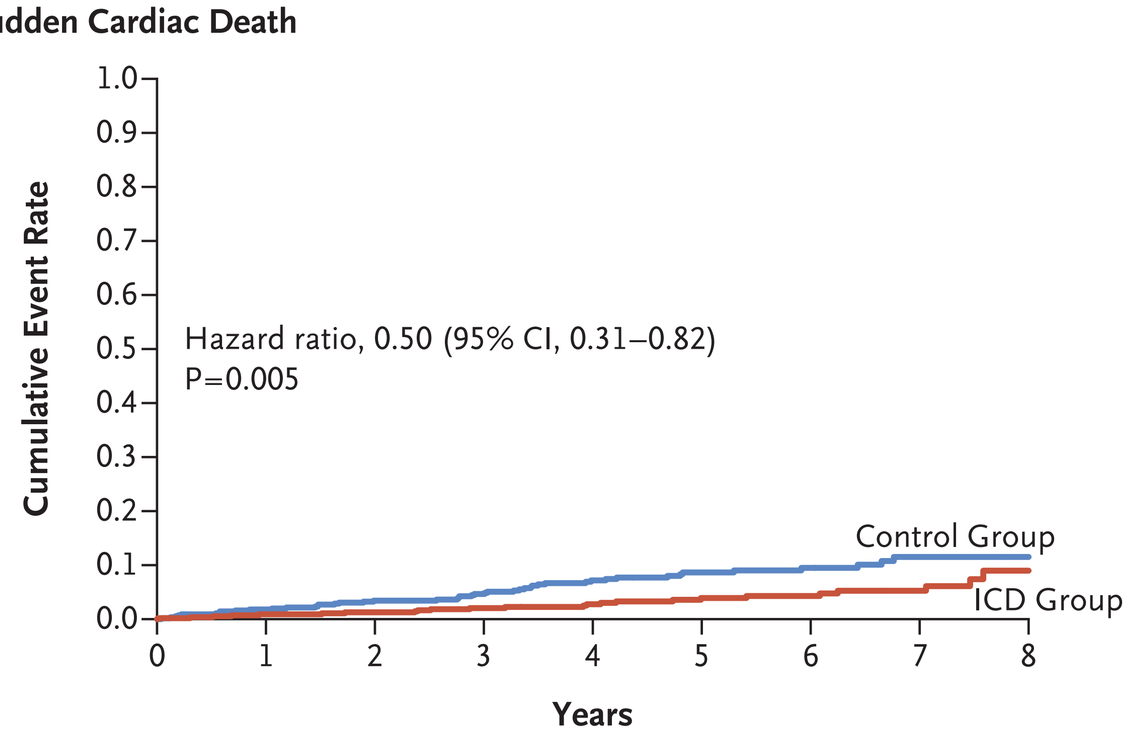
No. at Risk					
Defibrillator	742	503 (0.91)	274 (0.84)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Moss AJ et al; NEJM 2002

ICD in Patients with Nonischemic Systolic Heart Failure
DANISH

556 patients with symptomatic systolic heart failure (left ventricular ejection fraction, ≤35%) not caused by coronary artery disease were assigned to receive an ICD, and 560 patients were assigned to receive usual clinical care





Køber L et al: N Engl J Med 2016

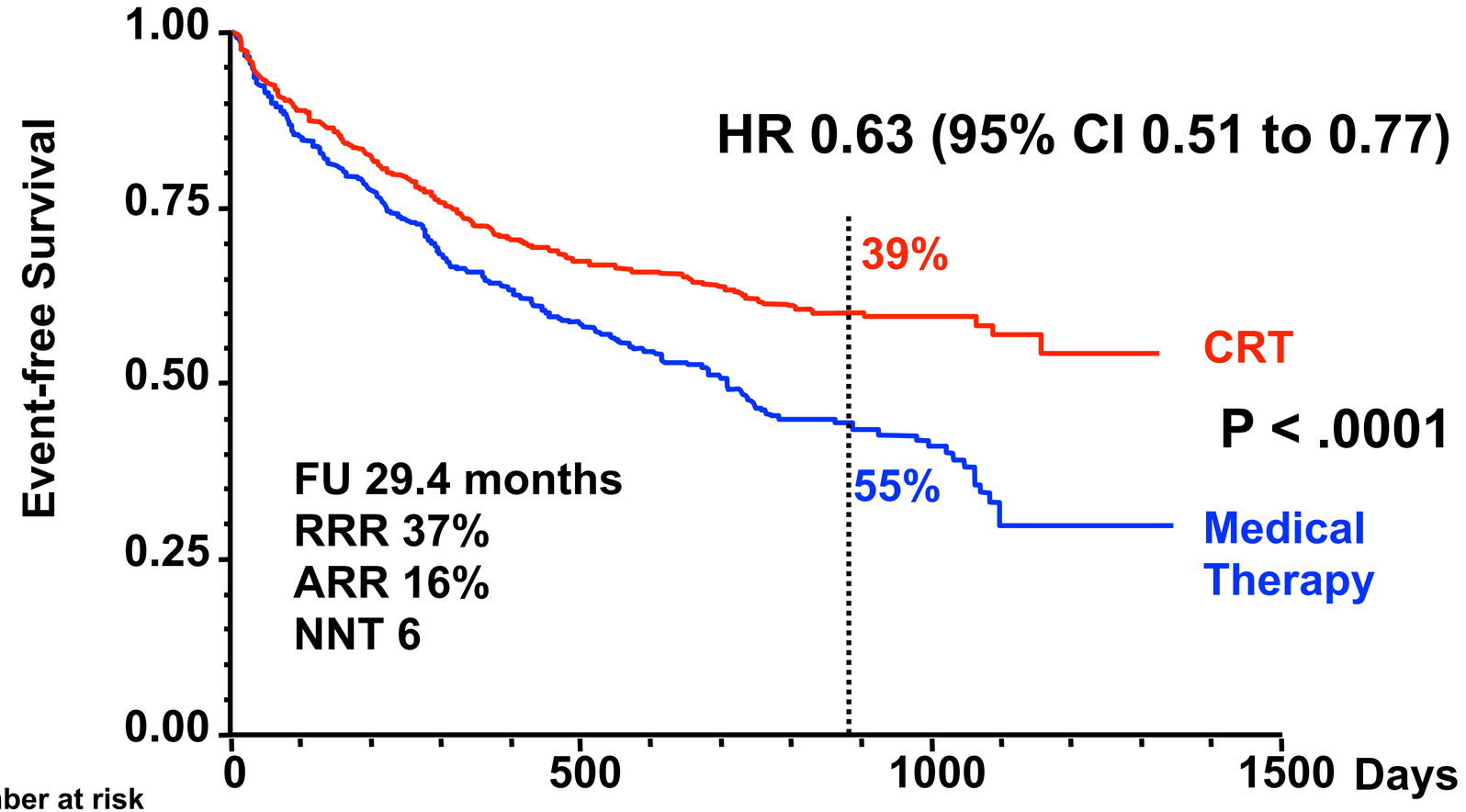
ICD in Patients with Nonischemic Systolic Heart Failure
DANISH

Subgroup	ICD Group	Control Group	Hazard Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no.				
Age					0.009
<59 yr	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 to <68 yr	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 yr	67/216	47/177	1.19 (0.81–1.72)	0.38	
Sex					0.66
Female	22/151	23/156	1.03 (0.57–1.87)	0.92	
Male	98/405	108/404	0.85 (0.64–1.12)	0.24	
NT-proBNP					0.06
<1177 pg/ml	32/266	74/268	0.59 (0.38–0.91)	0.02	
≥1177 pg/ml	57/292	88/290	0.99 (0.73–1.36)	0.96	
LV ejection fraction					0.69
<25%	70/264	65/242	0.87 (0.62–1.22)	0.42	
≥25%	50/292	66/318	0.79 (0.54–1.14)	0.21	
Estimated GFR					0.86
<73 ml/min/1.73 m^2	75/272	80/278	0.88 (0.64–1.21)	0.42	
≥73 ml/min/1.73 m^2	45/283	50/280	0.82 (0.55–1.23)	0.33	
NYHA functional class					0.71
II	52/297	54/300	0.92 (0.63–1.35)	0.68	
III–IV	68/259	77/260	0.81 (0.58–1.13)	0.21	
Cause of heart failure					0.80
Idiopathic	90/424	100/425	0.88 (0.66–1.17)	0.37	
Valvular	4/20	5/21	0.59 (0.13–2.71)	0.50	
Hypertension	13/62	12/55	0.68 (0.29–1.63)	0.39	
Other	13/50	14/59	1.02 (0.47–2.20)	0.96	
Preexisting pacemaker					0.71
No	108/500	120/514	0.88 (0.68–1.14)	0.34	
Yes	12/56	11/46	0.88 (0.36–2.20)	0.79	
CRT					0.73
No	58/234	65/237	0.83 (0.58–1.19)	0.31	
Yes	62/322	66/323	0.91 (0.64–1.29)	0.59	
Overall			0.87 (0.68–1.12)	0.28	

Køber L et al: N Engl J Med 2016

CARE-HF: Primary Endpoint

(All-cause Mortality or Unplanned Hosp. for Major CVS Event)



Number at risk						
CRT	409	323	273	166	68	7
Medical Therapy	404	292	232	118	48	3

Universität Zürich[UZH]

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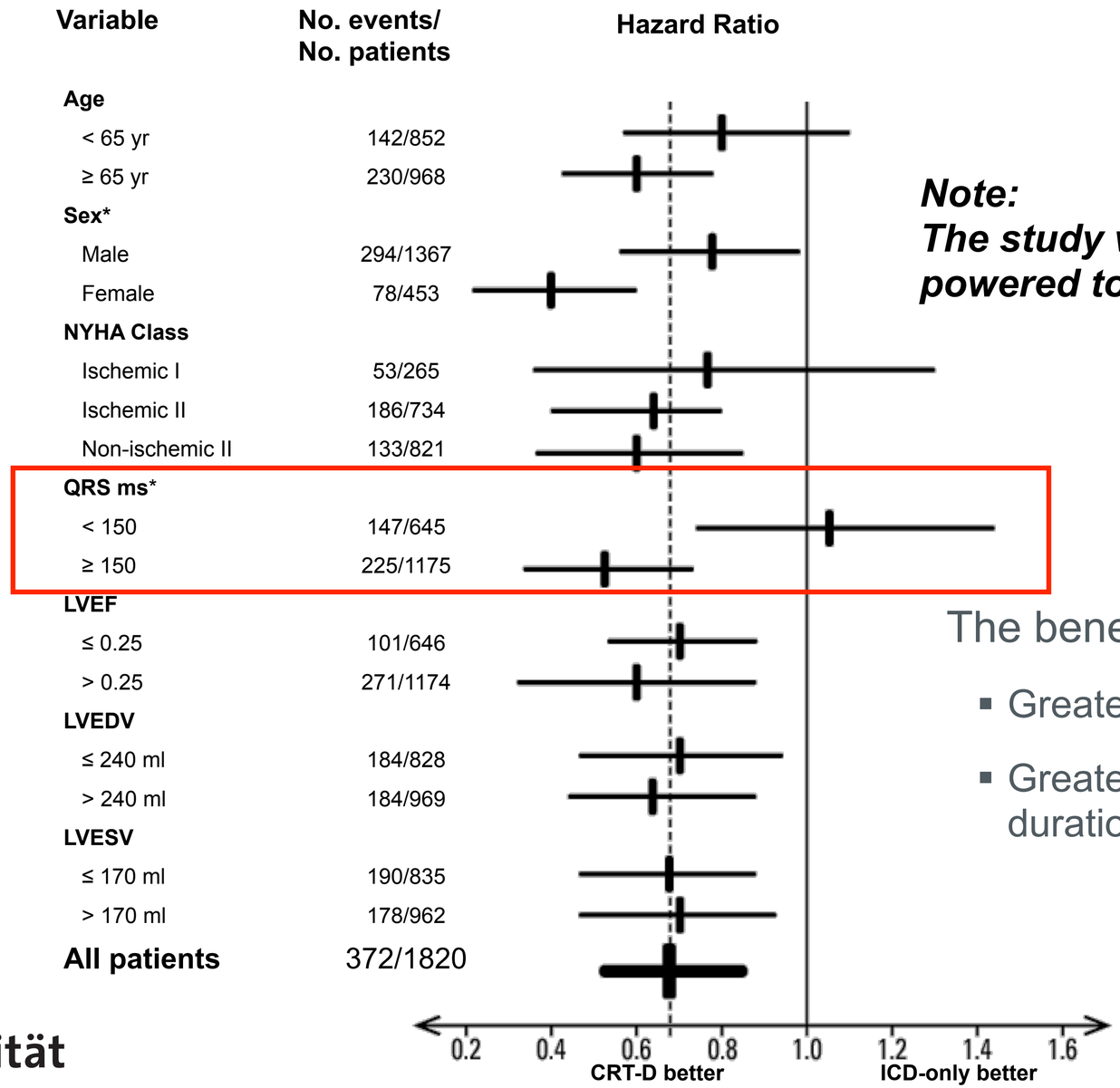
MADIT-CRT– Subgruppen



Note:
The study was not statistically powered to evaluate subgroups

The benefit of CRT-D appeared to be:

- Greater in women that in men
- Greater in patients with wider QRS duration

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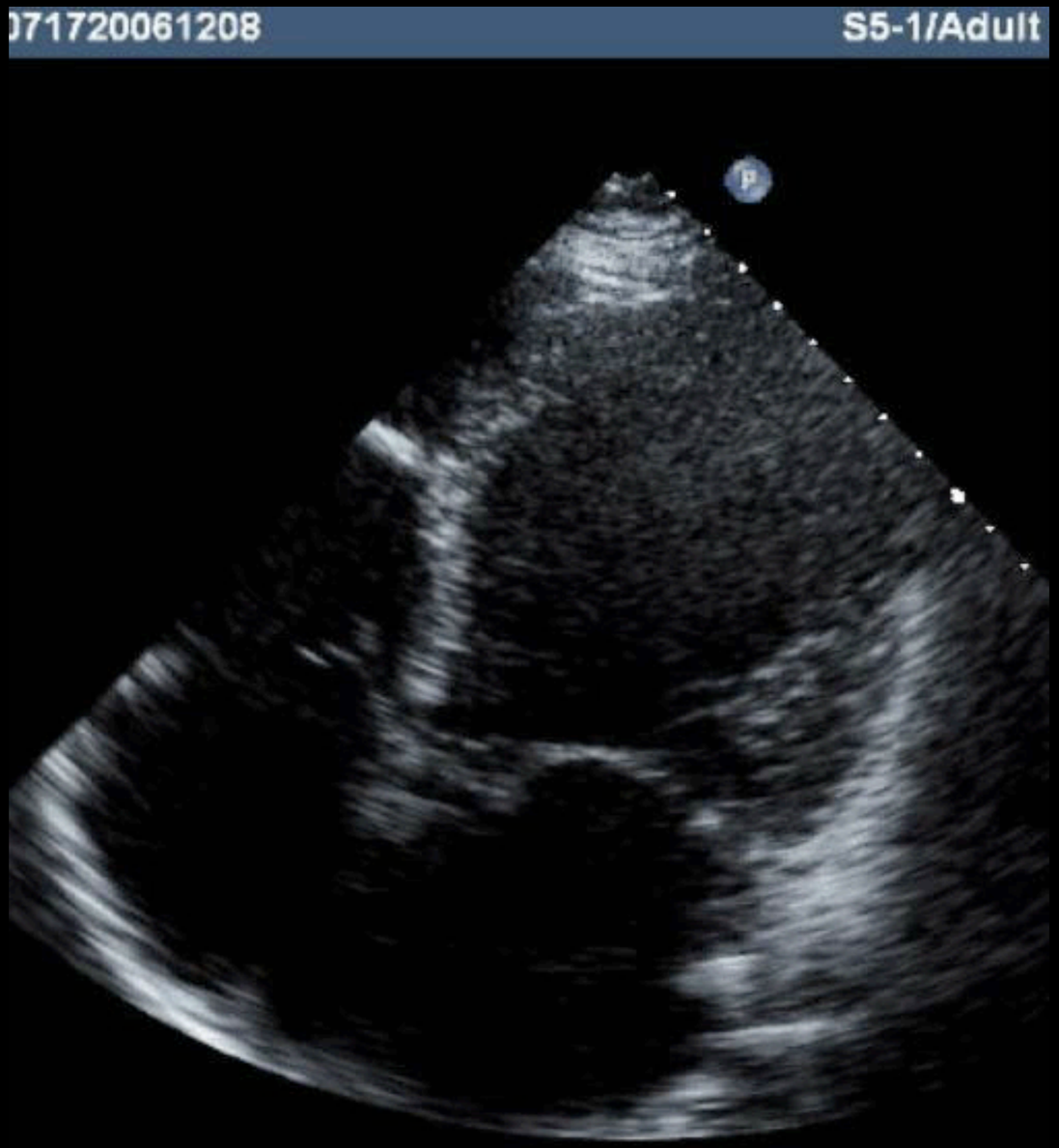
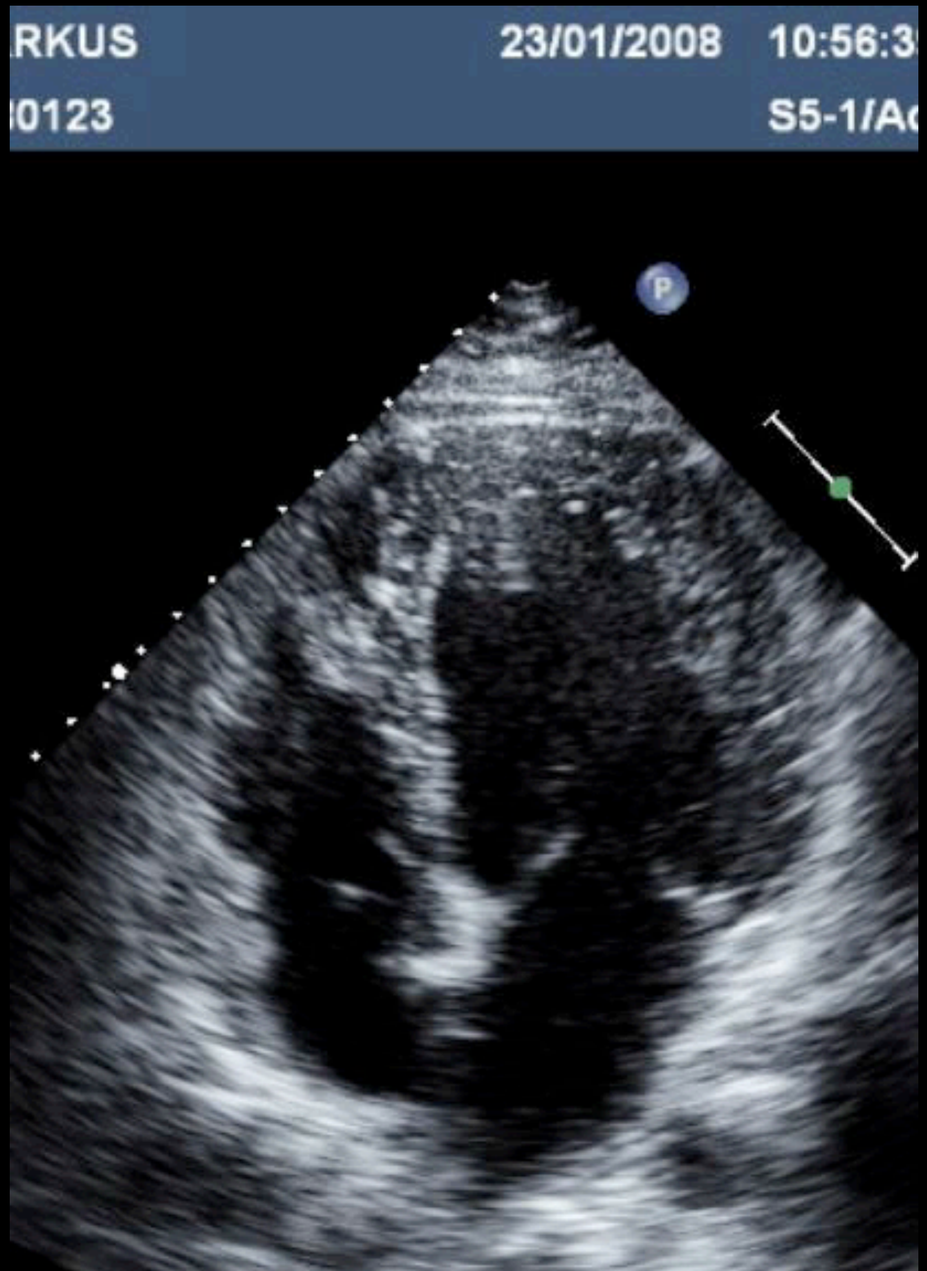
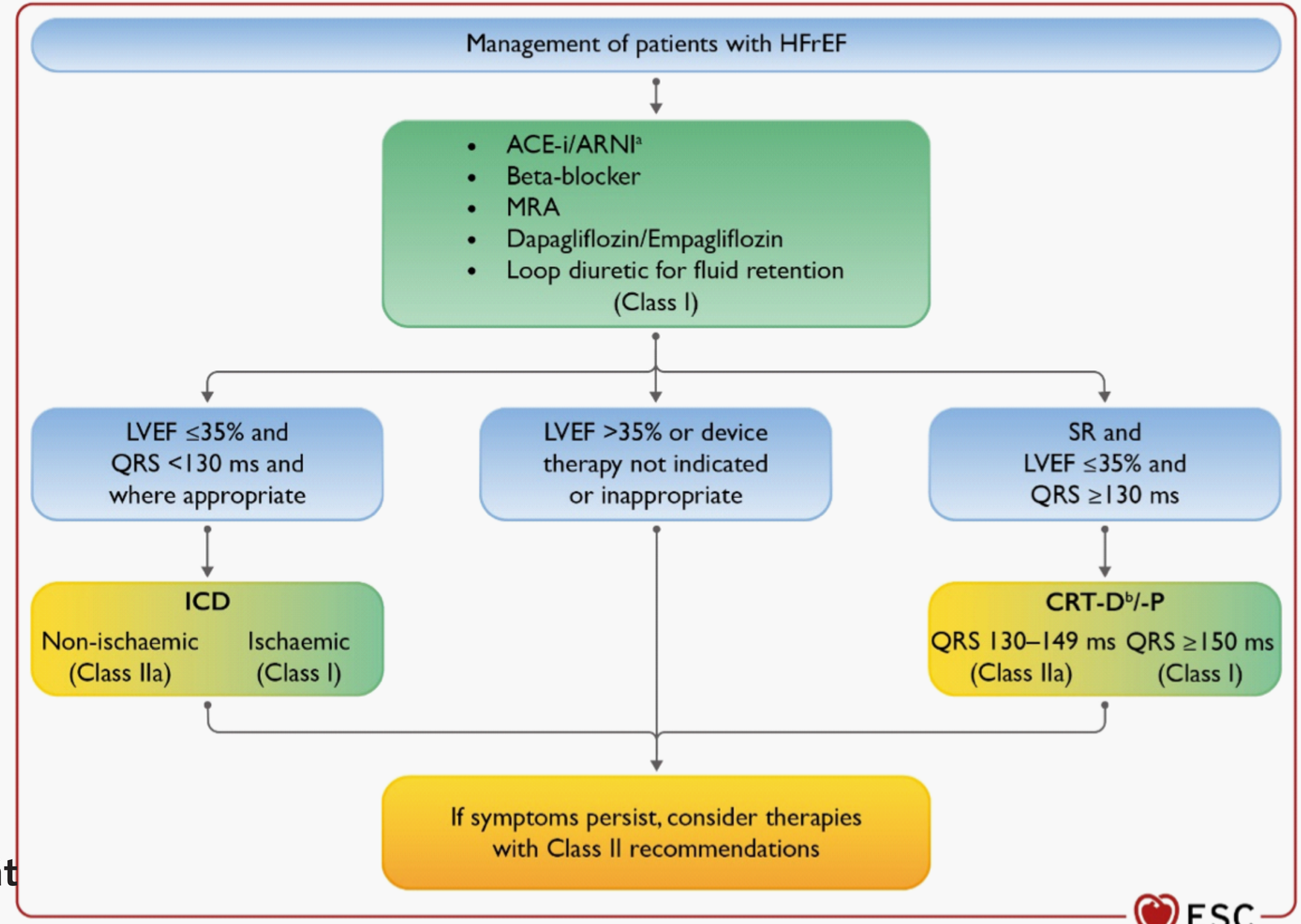
Moss AJ, Hall WJ, Cannom DS, et al. [serial online]. NEJM. Sept 2009

Resynchronisation





Therapeutic Algorithm of Class I Therapy in Patients with Heart Failure with Reduced Ejection Fraction



McDonagh TA et al: Eur Heart J 2021

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Catheter Ablation in End-Stage Heart Failure with Atrial Fibrillation

Christian Sohns, M.D., Henrik Fox, M.D., Nassir F. Marrouche, M.D., Harry J.G.M. Crijns, M.D., Ph.D., Angelika Costard-Jaeckle, M.D., Leonard Bergau, M.D., Gerhard Hindricks, M.D., Nikolaos Dagres, M.D., Samuel Sossalla, M.D., Rene Schramm, M.D., Ph.D., Thomas Fink, M.D., Mustapha El Hamriti, M.D., Maximilian Moersdorf, M.D., Vanessa Sciacca, M.D., Frank Konietschke, Ph.D., Volker Rudolph, M.D., Jan Gummert, M.D., Jan G.P. Tijssen, Ph.D., and Philipp Sommer, M.D., for the CASTLE HTx Investigators

27.08.2023

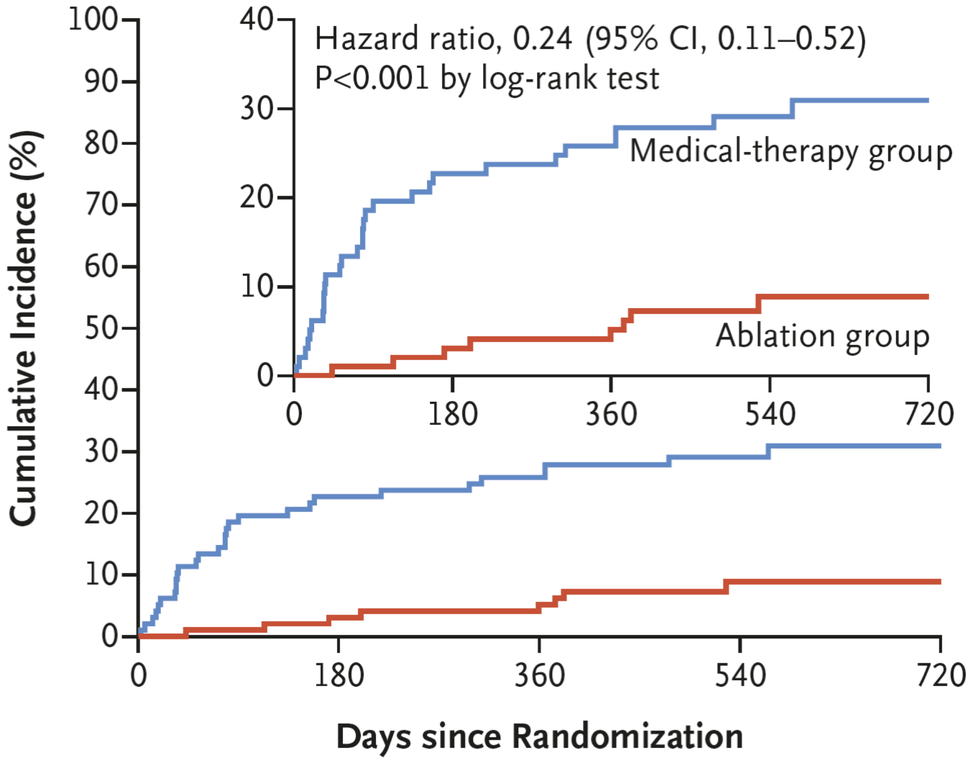
CASTLE-HTx - Baseline Characteristics

Characteristic	Ablation Group (N=97)	Medical-Therapy Group (N=97)
Age — yr	62±12	65±10
Male sex — no. (%)	85 (88)	72 (74)
Body-mass index†	28±4	28±5
NYHA functional class — no. (%)‡		
II	33 (34)	28 (29)
III	52 (54)	54 (56)
IV	12 (12)	15 (15)
Left ventricular ejection fraction — %	29±6	25±6
Type of atrial fibrillation — no. (%)		
Paroxysmal	28 (29)	31 (32)
Persistent	54 (56)	54 (56)
Long-standing persistent: duration of >1 yr	15 (15)	12 (12)
Duration of atrial fibrillation — yr	4±5	3±4
History of cardioversion — no. (%)	64 (66)	62 (64)
Heart rate — beats/min	80±21	82±20
Cause of heart failure — no. (%)		
Ischemic	37 (38)	39 (40)
Nonischemic	60 (62)	58 (60)
Left atrial diameter — mm	49±6	48±8

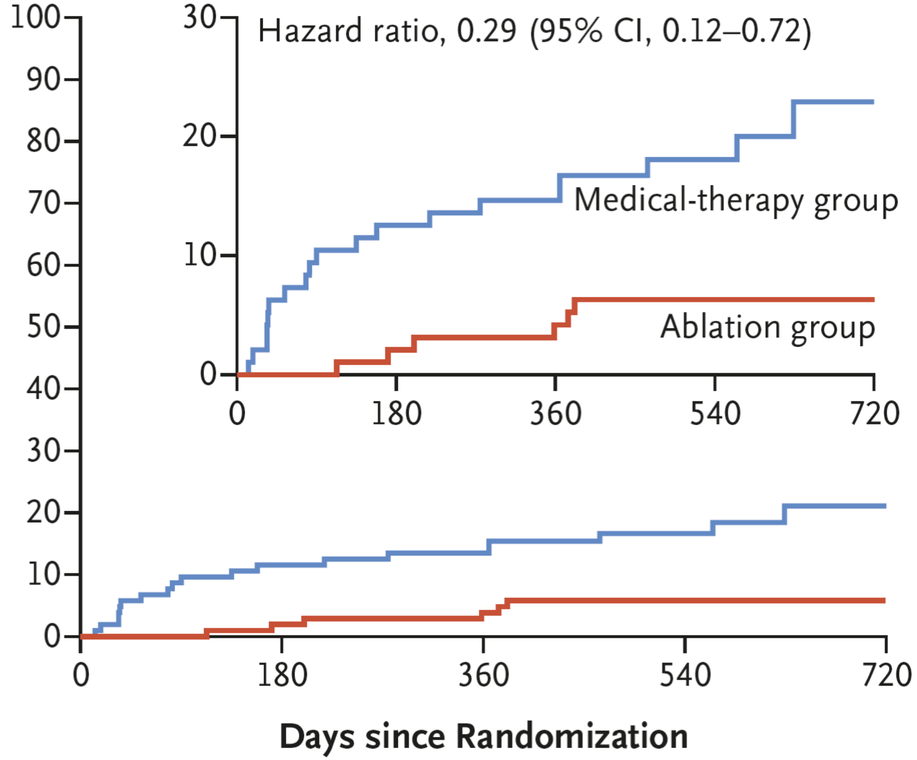
Sohns et al., NEJM 2023

CASTLE-HTx - Results

Death from any cause, implantation of a LVAD, urgent HTX



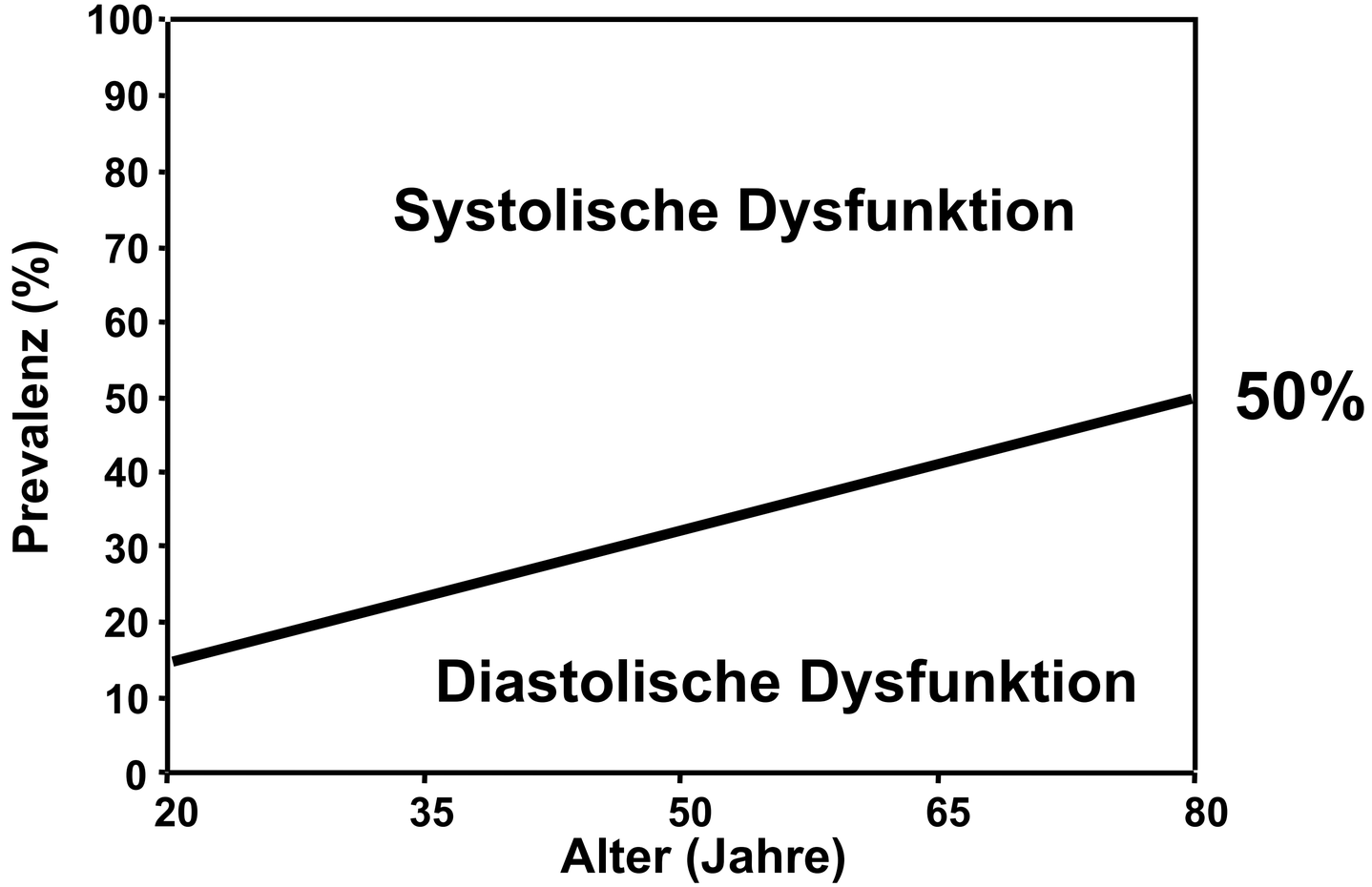
Death from any cause



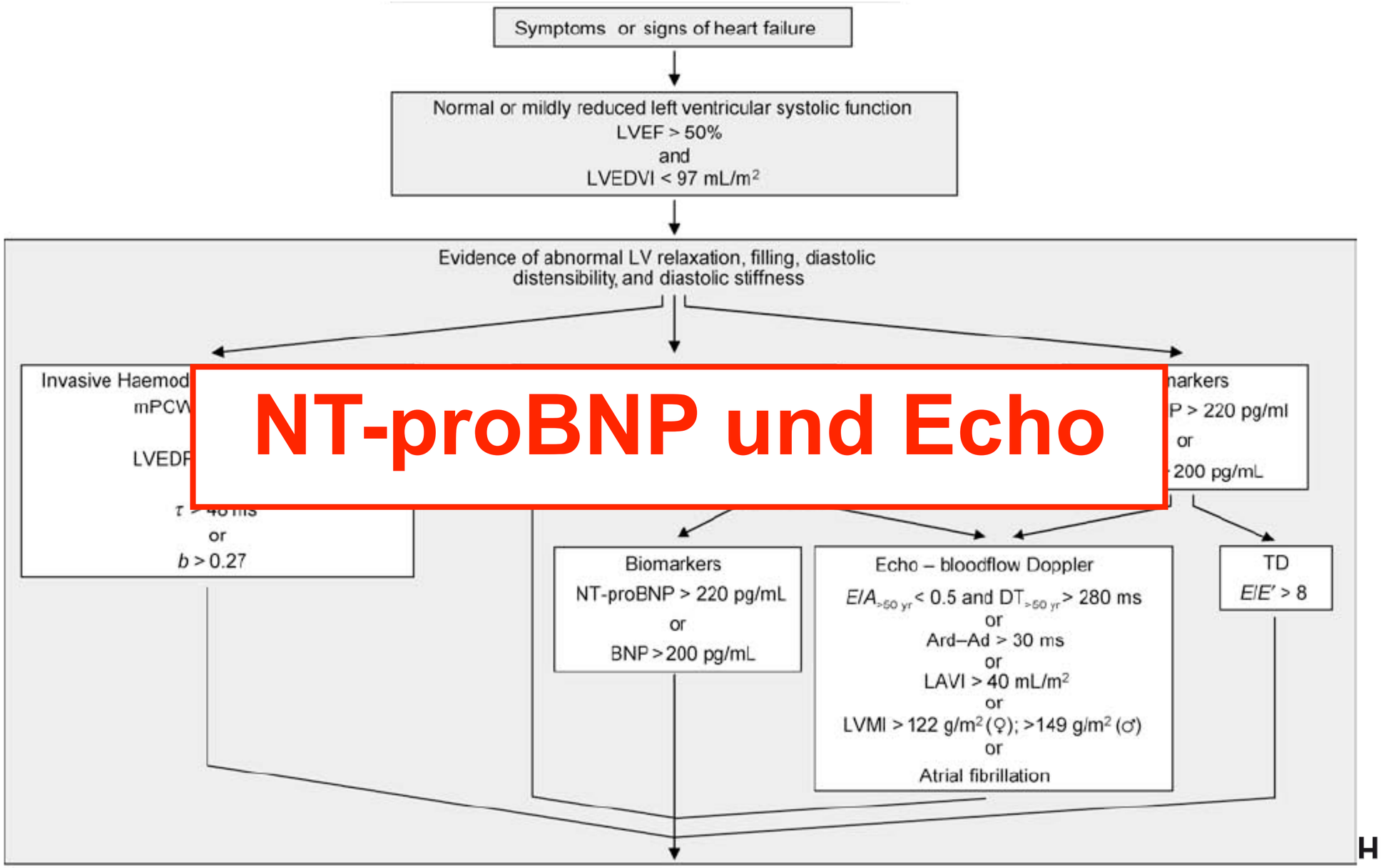
No. at Risk										
Medical-therapy group	97	75	72	41	12	97	85	83	45	13
Ablation group	97	94	88	50	20	97	95	93	51	20

Sonns et al., NEJM 2023

Prevalenz von systolischer/diastolischer Dysfunktion als Ursache für eine Herzinsuffizienz



How to Diagnose HFpEF?



Paulus et al. *Eur Heart J* 2007

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Therapie der Herzinsuffizienz mit erhaltener systolischer Funktion

Behandlung der Hypertonie

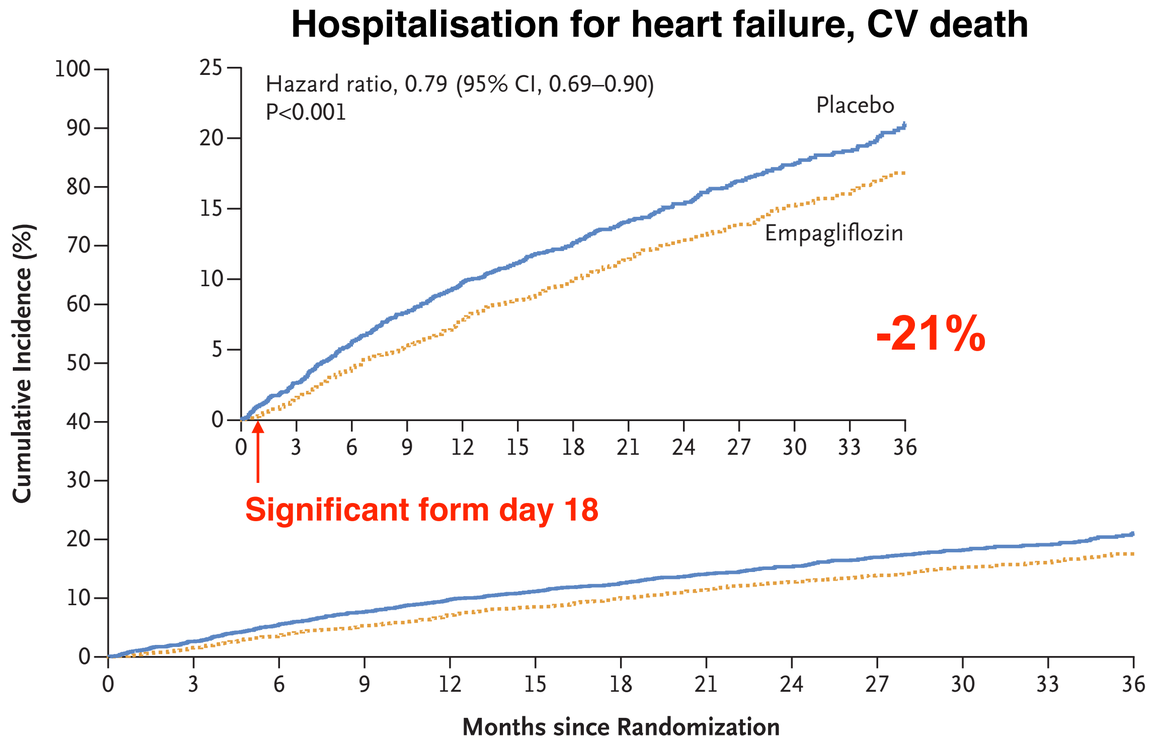
Suche bzw. Therapie einer Ischämie

Kontrolle von Vorhofflimmern

Diuretika (Spironolacton [TOPCAT])

SGLT2 Inhibitors in Patients with Preserved or Slightly Reduced LV Function

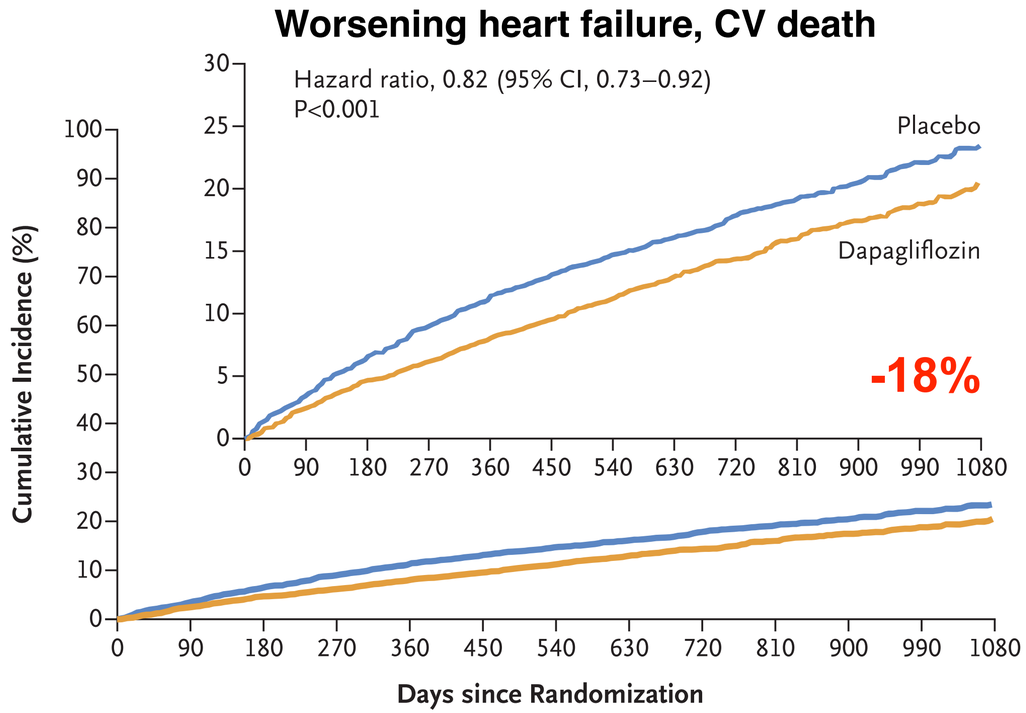
EMPEROR-Preserved



No. at Risk													
Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

Anker SD et al: NEJM 2021

DELIVER



No. at Risk													
Placebo	3132	3007	2896	2799	2710	2608	2318	2080	1923	1554	1140	772	383
Dapagliflozin	3131	3040	2949	2885	2807	2716	2401	2147	1982	1603	1181	801	389

Solomon SD et al: NEJM 2021

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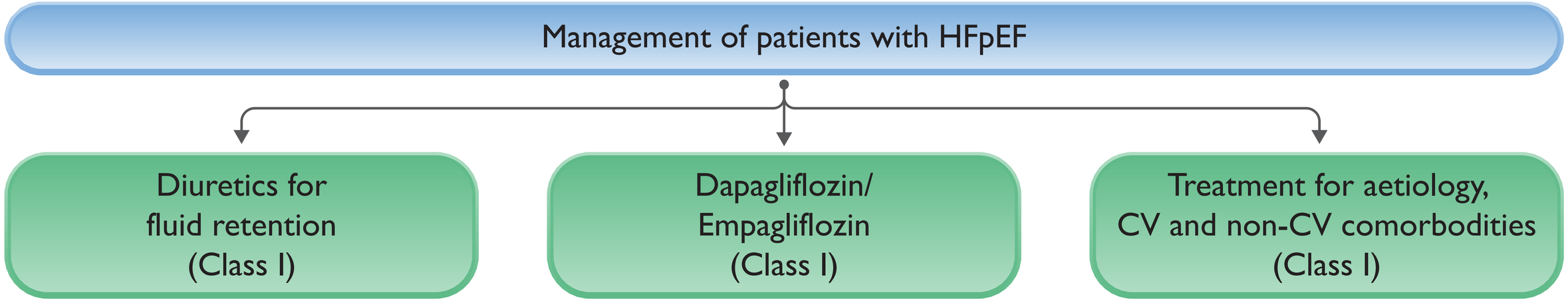
Management of Patients with HFpEF (EF ≥ 50%)



McDonagh TA et al: Eur Heart J 2023

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ORIGINAL ARTICLE

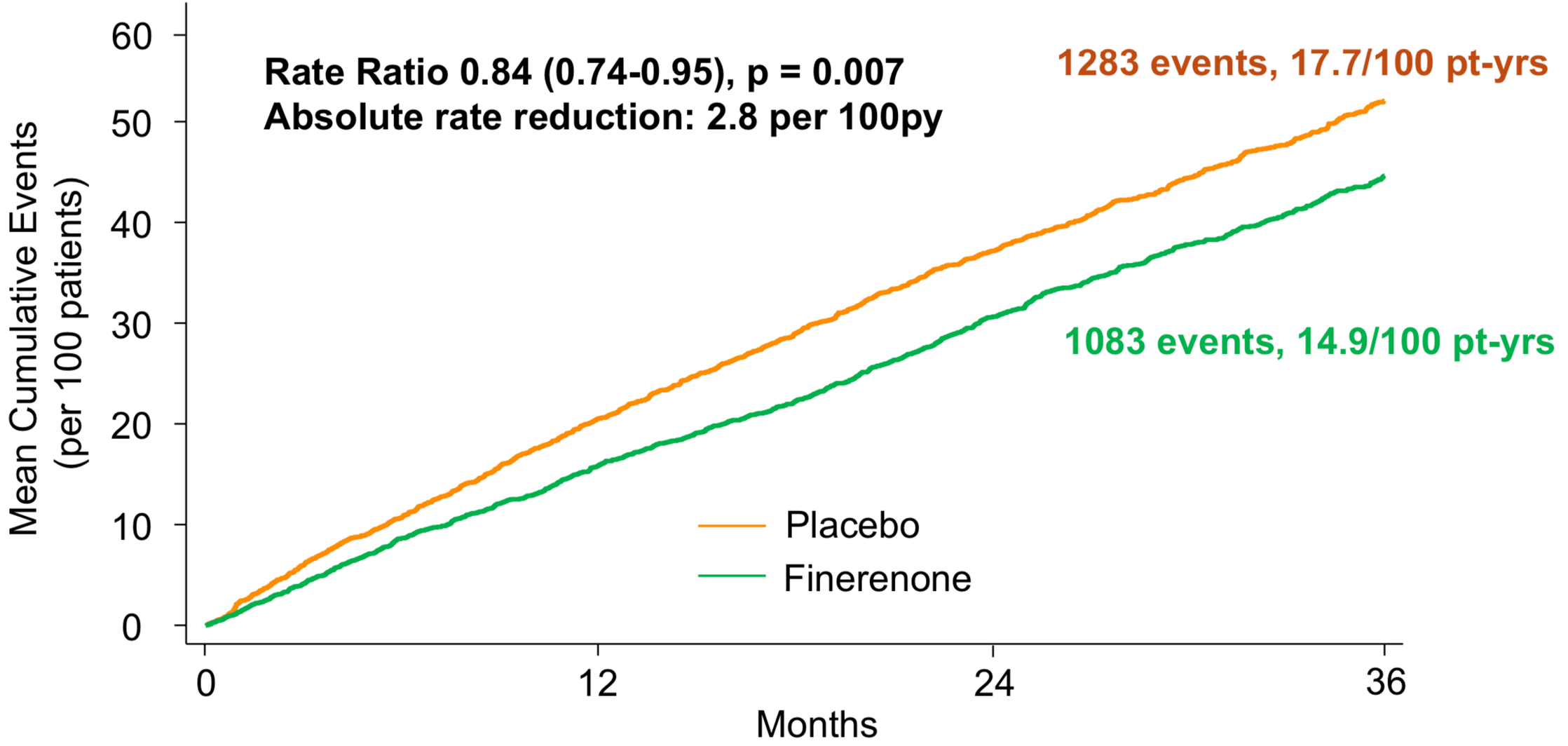
Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, M. Vaduganathan, B. Claggett, P.S. Jhund, A.S. Desai, A.D. Henderson, C.S.P. Lam, B. Pitt, M. Senni, S.J. Shah, A.A. Voors, F. Zannad, I.Z. Abidin, M.A. Alcocer-Gamba, J.J. Atherton, J. Bauersachs, M. Chang-Sheng, C.-E. Chiang, O. Chioncel, V. Chopra, J. Comin-Colet, G. Filippatos, C. Fonseca, G. Gajos, S. Goland, E. Goncalvesova, S. Kang, T. Katova, M.N. Kosiborod, G. Latkovskis, A.P.-W. Lee, G.C.M. Linssen, G. Llamas-Esperón, V. Mareev, F.A. Martinez, V. Melenovský, B. Merkely, S. Nodari, M.C. Petrie, C.I. Saldarriaga, J.F.K. Saraiva, N. Sato, M. Schou, K. Sharma, R. Troughton, J.A. Udell, H. Ukkonen, O. Vardeny, S. Verma, D. von Lewinski, L. Voronkov, M.B. Yilmaz, S. Zieroth, J. Lay-Flurrie, I. van Gameren, F. Amarante, P. Kolkhof, and P. Viswanathan, for the FINEARTS-HF Committees and Investigators*

NEJM 01.09.2024

FINEARTS-HF - Primary Endpoint: CV death and total HF events

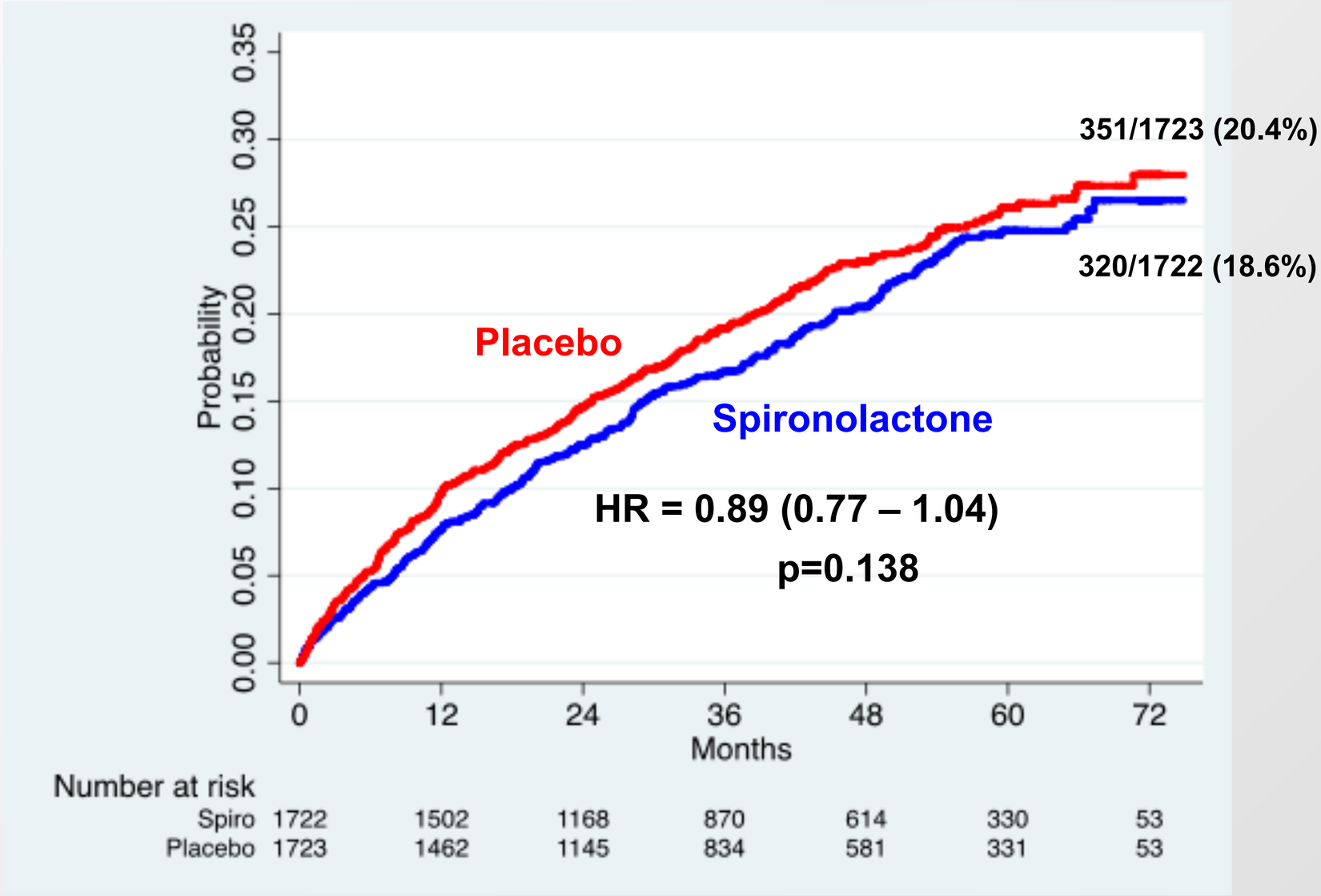
Finenerone reduced cardiovascular deat and total worsening heart failure events over median follow-up of 32 months



1°Outcome

(CV Death, HF Hosp, or Resuscitated Cardiac Arrest)

TOPCAT
Funded by the NHLBI



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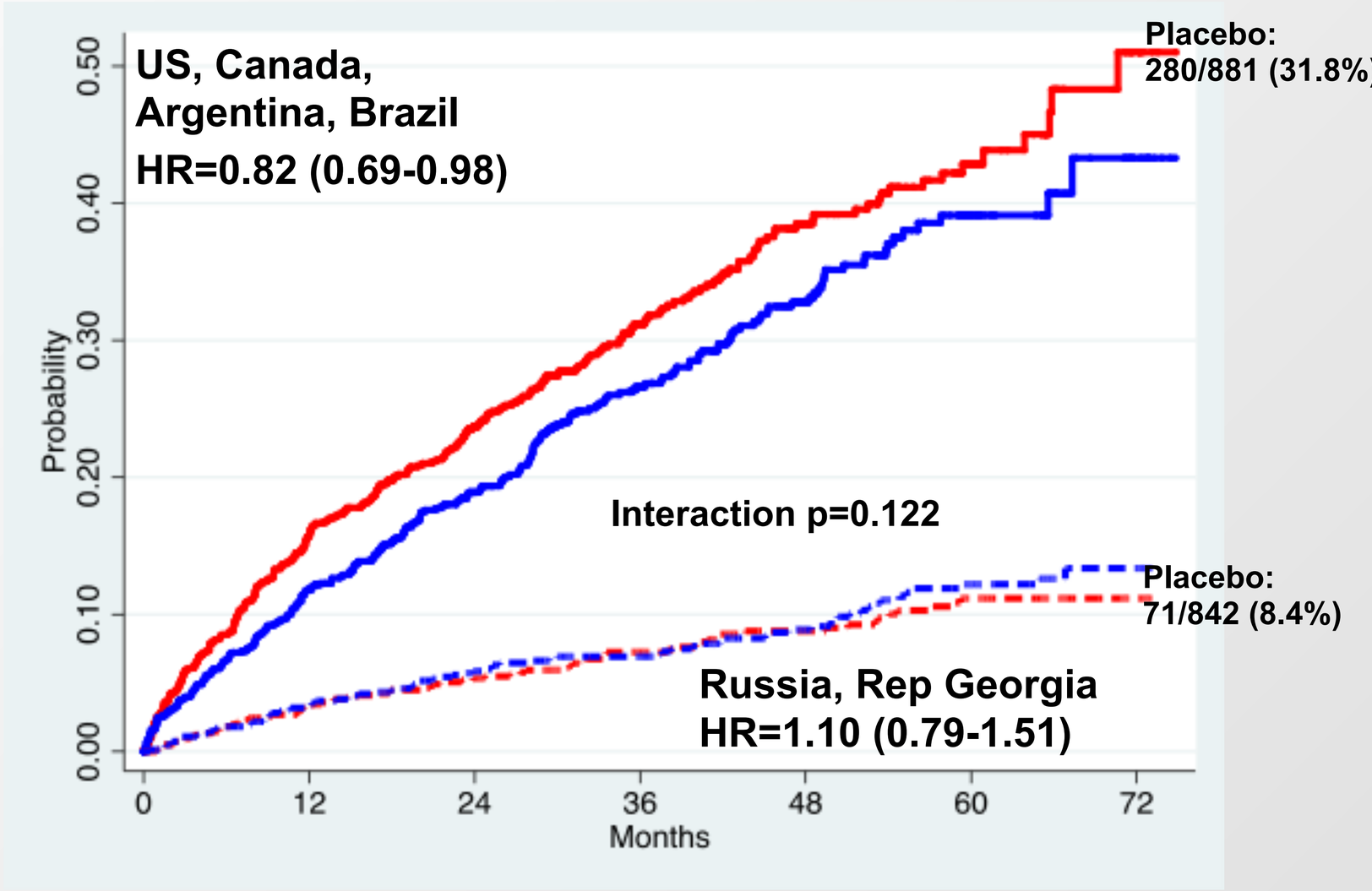
Exploratory (post-hoc): Placebo vs. Spiro by region

TOPCAT
Funded by the NHLBI



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Praktische Überlegungen für die optimale medikamentöse Herzinsuffizienzbehandlung

Problem	Lösung
Tiefer Blutdruck	– Unnötige Blutdruck-wirksame Medikamete reduzieren,
Or	ben

„If a patient is unable to tolerate maximal doses of all medications, lower doses of all medications are preferred over a high-dose therapy of one and no coverage of other pathways.“

Blutdruck- und Herzfrequenz-Ziele	– Zielwerte anstreben – Symptome sind prioritär vor hämodynamischen Werten
Müdigkeit	– Betablocker abends verabreichen – Wichtigkeit der Medikation erklären

Marti CN et al: Eur J Heart Fail 2019

ESC European Society of Cardiology
European Heart Journal (2023) **00**, 1–124
https://doi.org/10.1093/eurheartj/ehad194

2023 ESC Guidelines for the management of cardiomyopathies

- Phänotypische Charakterisierung: Echo, MR, Szintigraphie
- Ätiologien abklären: Bildgebung, Labor, Genetik
- Risikostratifizierung: Langzeit-EKG, MR, Genetik
- Therapie: Allgemein, spezifisch

Arbelo E et al: Eur Heart J 2023

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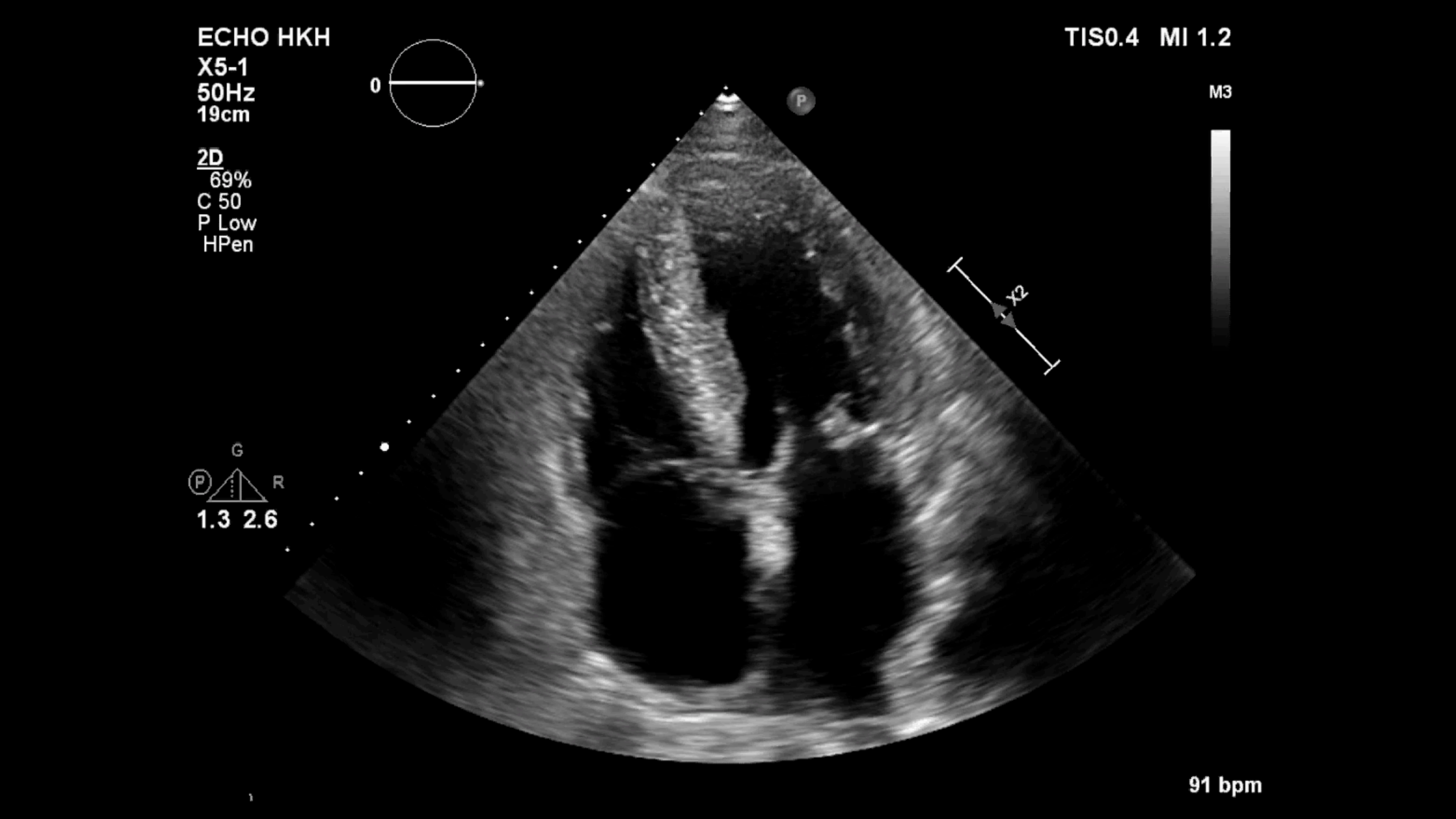
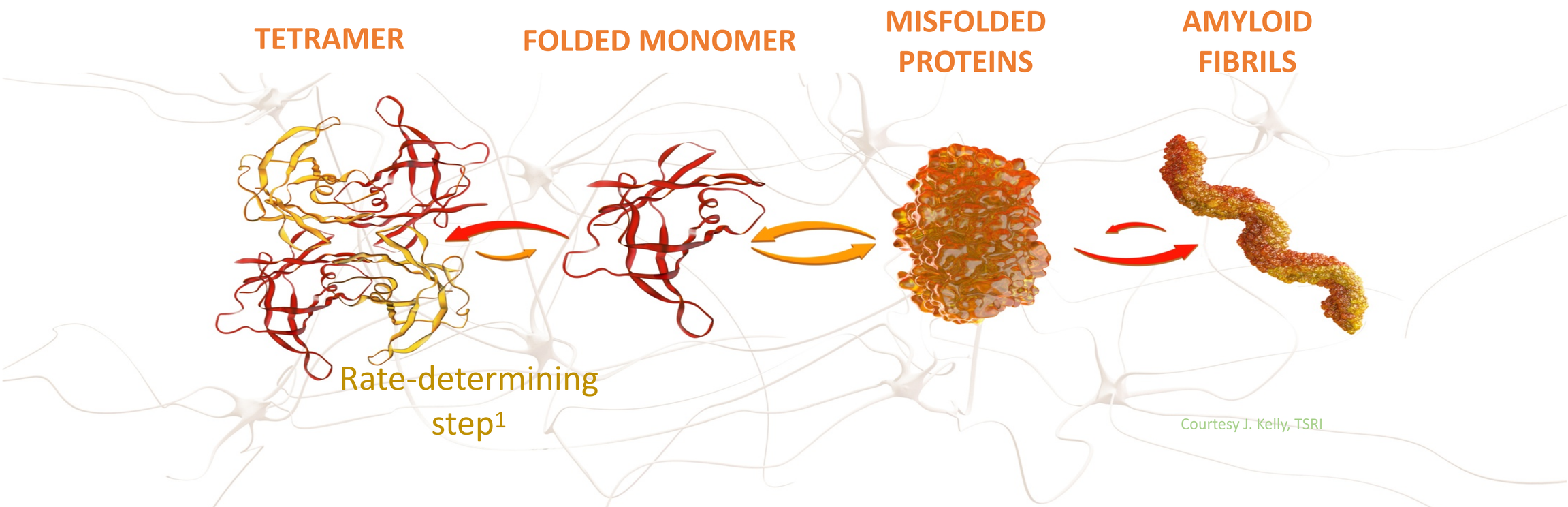

ECHO HKH
X5-1
50Hz
19cm
2D
69%
C 50
P Low
HPen
TIS0.4 MI 1.2
M3
X2
G
P
R
1.3 2.6
91 bpm

Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

Transthyretin tetramer destabilization leads to misfolded proteins that form amyloid fibrils.[1–3]



Pathogenic transthyretin variants alter the rate at which tetramers dissociate due to the effect of the mutation on the tetramer's stability.[1,2]

1.Hammarström P et al. *Science.* 2003;299:713–716. 2.Sekijima Y et al. *Curr Pharm Des*. 2008;14:3219–3230. 3.Benson MD et al. *Mus Nerve* 2007;36:411–423.

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Cardiac Amyloidosis

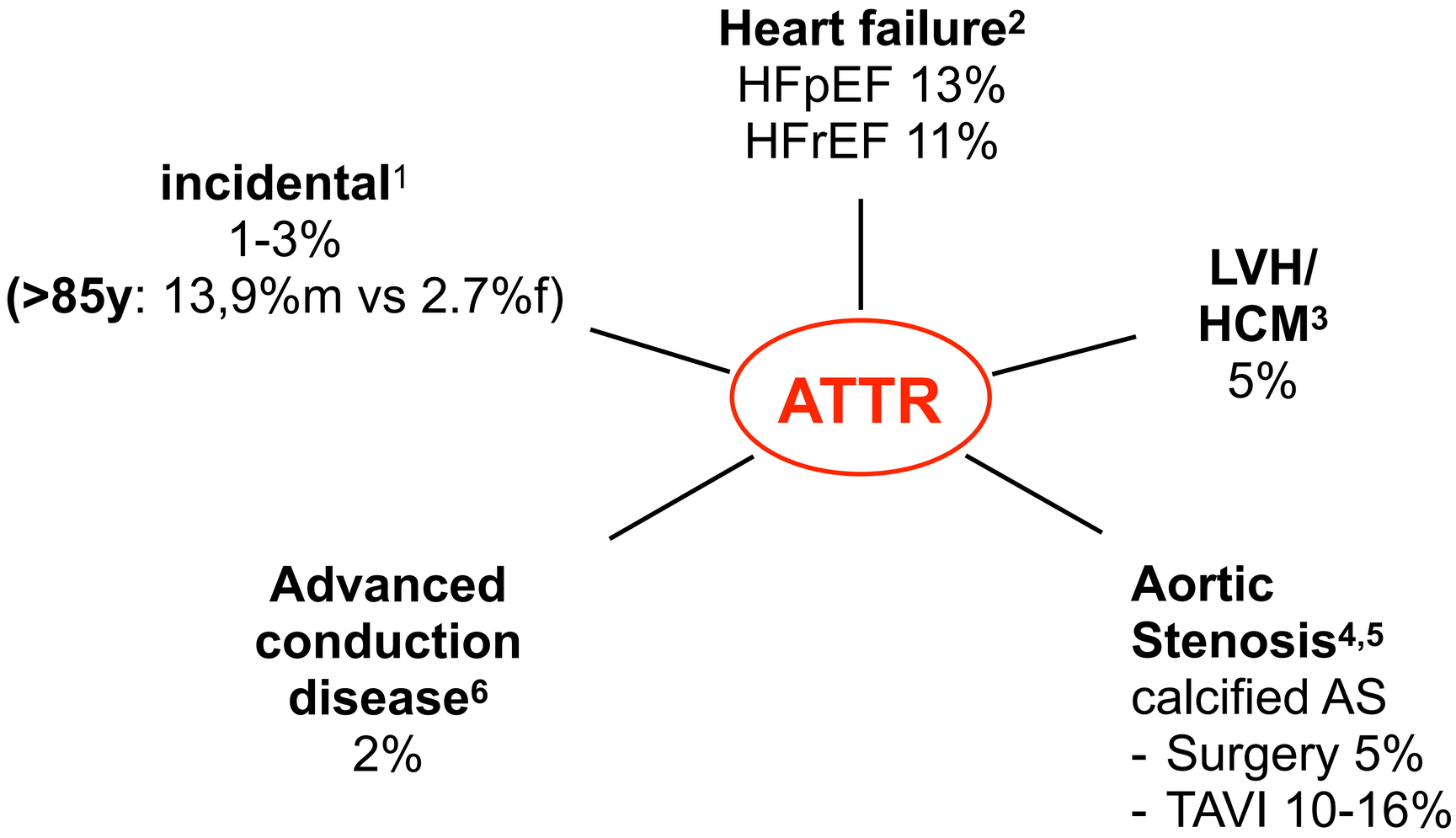
Extracellular deposition of misfolded pathologic proteins int the myocardium

AL Amyoidosis (light chain amyloidosis)
- Kappa/lambda light chains (blood)
- Immunfixation (blood, urine)

ATTR Amyoloidosis
- Wild type (senile)
- Hereditary (genetic testing)
- Tc-Scintigraphy

Red Flags
- Heart failure
- ECG (low voltage)
- „LVH“
- Carpal tunnel syndrome
- Autonomic dysfunction

ATTR-CM: rare, but not too rare



1.Mohammed-Salem L. et al (2018), *Int J Cardiol*; 2. González-López E et al (2015), *Eur Heart J*; 3. Thibeau D. et al (2015), *Eur Heart J*; 4. Castano A. et al (2017), *Eur Hear J*; 5. Treibel T. et al (2016), *Circ Cardiovasc Imaging* 6. González-Lopez E. et al (2019), *Amyloid*

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Therapie der ATTR-Amyloidose

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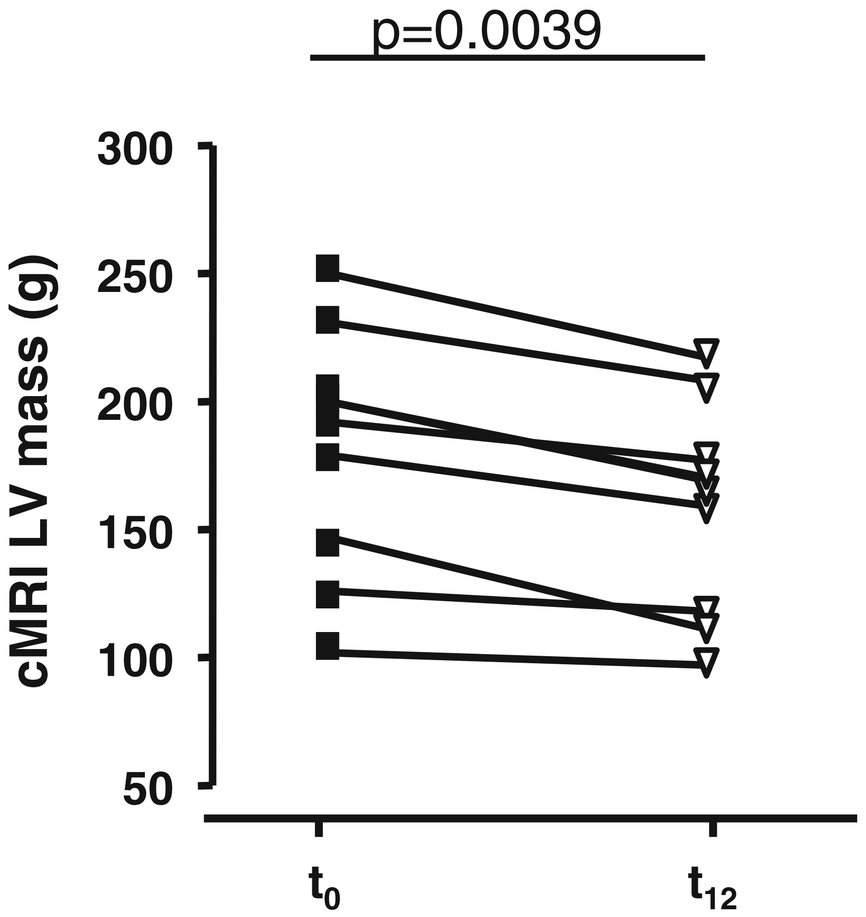
Green tea halts progression of cardiac transthyretin amyloidosis: an observational report

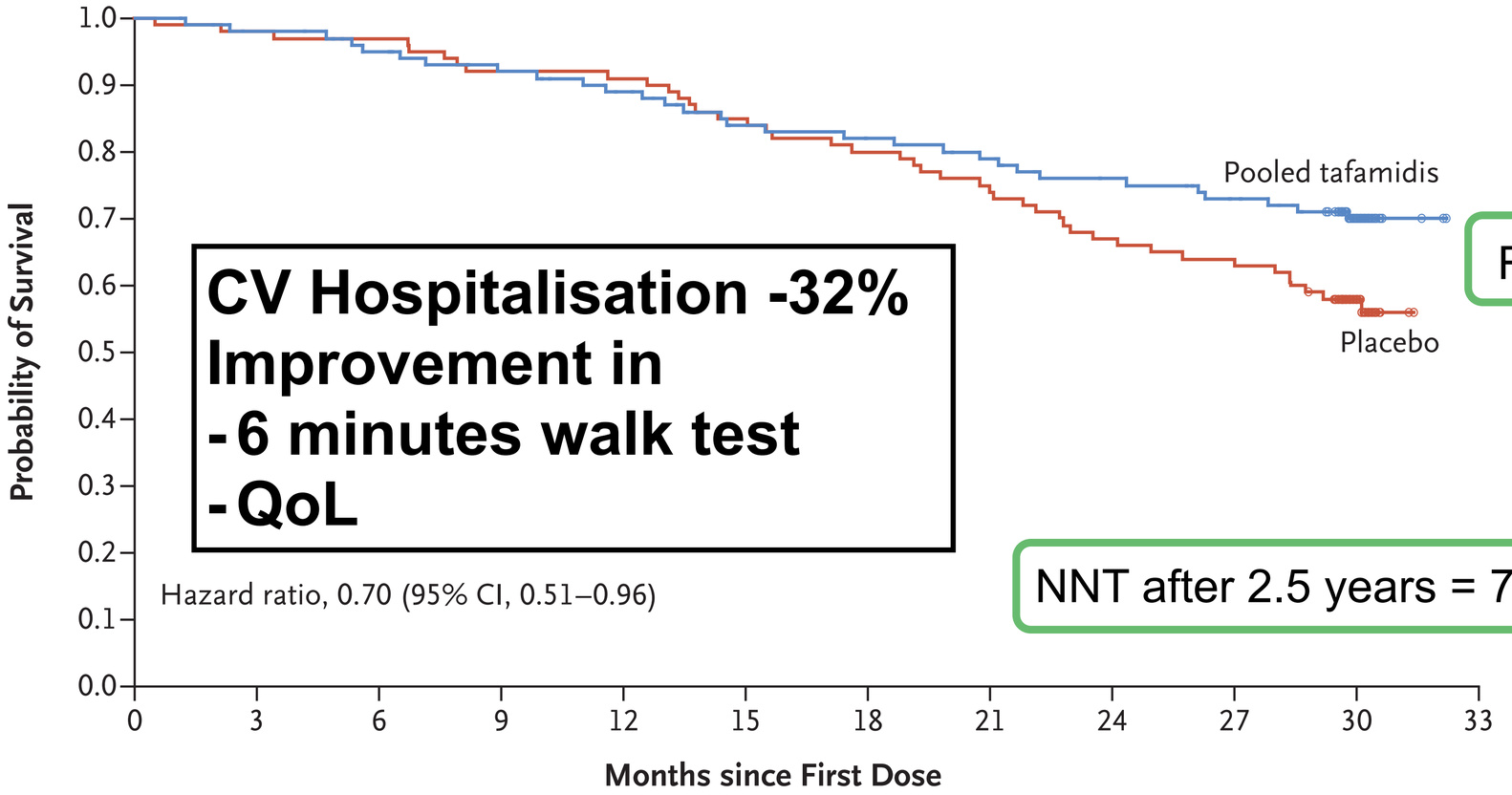
Arnt V. Kristen · Stephanie Lehrke · Sebastian Buss · Derliz Mereles · Henning Steen · Philipp Ehlermann · Stefan Hardt · Evangelos Giannitsis · Rupert Schreiner · Uwe Haberkorn · Philipp A. Schnabel · Reinhold P. Linke · Christoph Röcken · Erich E. Wanker · Thomas J. Dengler · Klaus Altland · Hugo A. Katus



Clin Res Cardiol 2012

HERZKLINIK HIRSLANDEN

ATTR-ACT: All-Cause Mortality



CV Hospitalisation -32%
Improvement in
- 6 minutes walk test
- QoL

RRR 30%

NNT after 2.5 years = 7.5[2]

No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

30% reduction in the risk of all-cause mortality with tafamidis compared with placebo (HR = 0.70; 95% CI, 0.51 – 0.96)[1]
33% reduction when heart transplant and implantation of a cardiac mechanical assist device were not treated as death (HR = 0.67; 95% CI, 0.49 – 0.94)[1]

1. Maurer, M. S., et al. *N Engl J Med* 2018;379:1007-1016; 2. Maurer, M. S., et al. *JACC Basic Transl Sci* 2018;3:871-873

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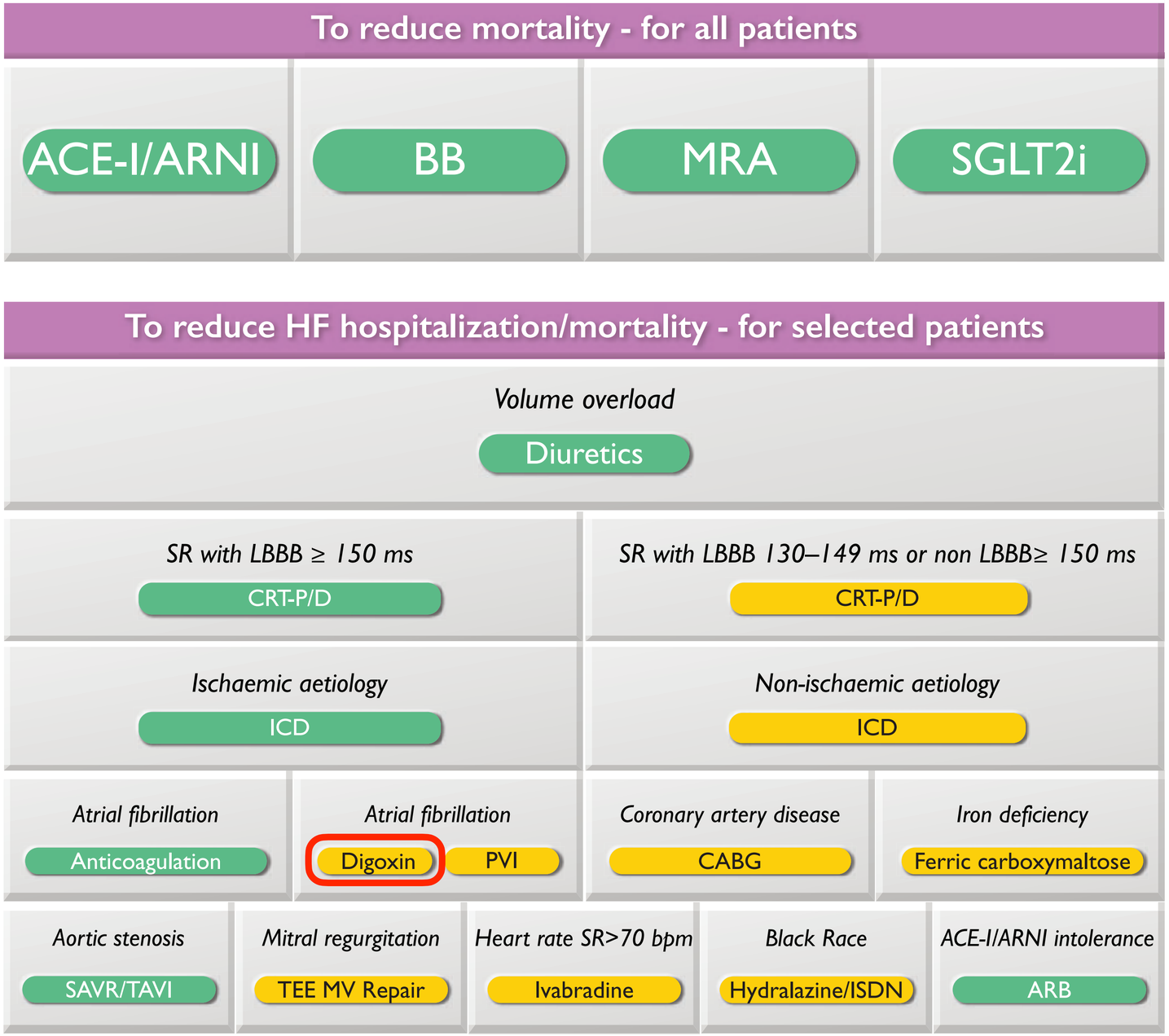
Management of HFrEF



McDonagh TA et al: Eur Heart J 2021

Universität Zürich[UZH]

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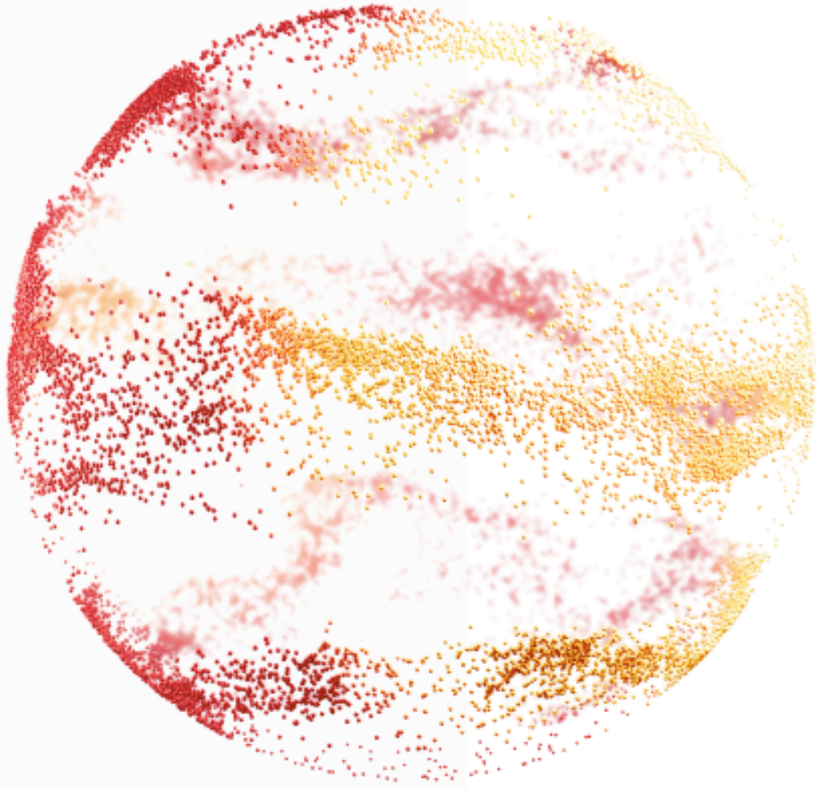
NEWS from

ESC Congress 2025 Madrid

TOGETHER WITH

World Congress of Cardiology

29 August to 1 September



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Digitoxin in Patients with Heart Failure and Reduced Ejection Fraction

U. Bavendiek,[1] A. Großhennig,[2] J. Schwab,[3,4] D. Berliner,[1] A. Rieth,[5] L.S. Maier,[6] T. Gaspar,[7,8] N.H. Thomas,[2] X. Liu,[2] S. Schallhorn,[1] E. Angelini,[1] S. Soltani,[1] F. Rathje,[1] M.-A. Sandu,[1] W. Geller,[1] R. Hambrecht,[9] M. Zdravkovic,[10] S. Philipp,[11] D. Kosevic,[12] G. Nickenig,[13] D. Scheiber,[14] S. Winkler,[15] P.M. Becher,[16-18] P. Lurz,[19] M. Hülsmann,[20] S. Wiesner,[2] C. Schröder,[21] B. Neuhaus,[22] A. Seltmann,[22] H. von der Leyen,[23,24] C. Veltmann,[1,25] S. Störk,[26,27] M. Böhm,[28] A. Koch,[2] and J. Bauersachs,[1] for the DIGIT-HF Study Group*

29.08.2025

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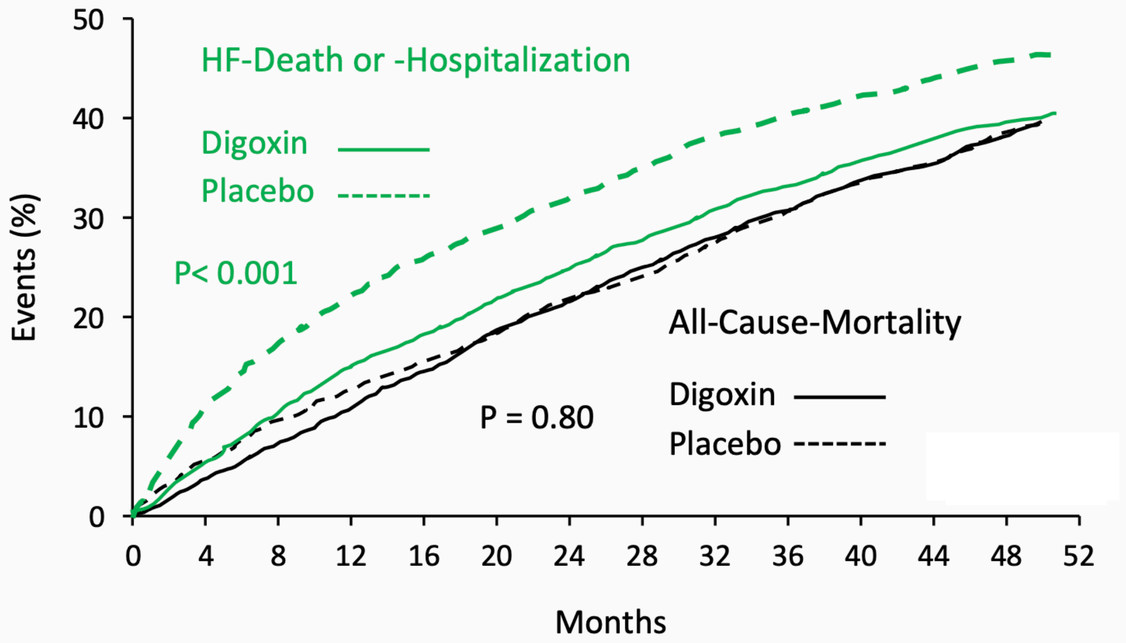
Background

DIG trial



Worsening HFH: Risk Ratio 0.72 (0.66-0.79), p<0.001

Bavendiek U, Bauersachs J, ESC Textbook of Heart Failure 2023
Adapted from DIG Invesigators NEJM 1997, 336:525

Potential benefit particularly if
- LVEF <25%
- NYHA III/IV
- Digoxin 0.5-0.9 ng/ml

Digoxin > 1.0 ng/ml
- association with worse outcomes

Digitoxin
- more stable serum concentrations even if worsening renal function
- no clinical trials of appropiate size

Rathore SS et al., JAMA 2003, 289:871
Belz GG, Eur J Clin Invest 2001, 31(2):10
Gheorghiade M et al. , EJHF 2013, 15:551

With funding from the:
Federal Ministry of Research, Technology and Space

Study design and recruitment

DIGIT-HF

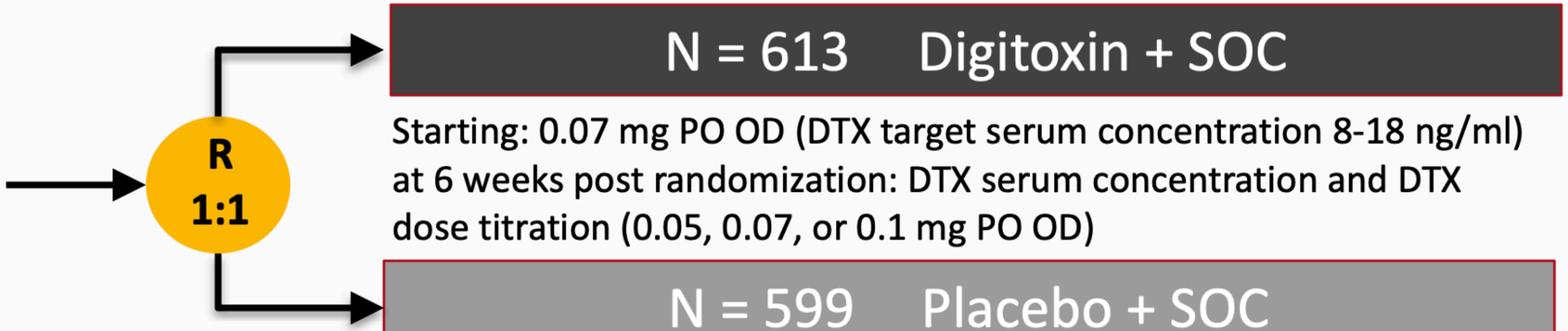
investigator-initiated, multicentre, randomized, double-blind, placebo-controlled, event-driven phase IV trial investigating wether digitoxin improves outcomes in patients with heart failure and reduced ejection fraction

Main inclusion criteria
- Chronic HF
- NYHA II and LVEF ≤30%
  or
  NYHA III-IV and LVEF ≤40%
- Evidence based HF therapy
  ≥ 6 months

Main exclusion criteria
- Amiodarone
- Heart rate < 60 b.p.m
  (except CRT-in place)
- Recent (< 2 month)
  procedure potentially
  improving LVEF/HF

Randomization of 1240 patients (05/2015 – 09/2023, LPLV 29.11.2024,
55 sites: Germany 89%, Austria 3%, Serbia 8%)

Intention to treat population: n= 1212 (at least one dose of IMP)



Starting: 0.07 mg PO OD (DTX target serum concentration 8-18 ng/ml) at 6 weeks post randomization: DTX serum concentration and DTX dose titration (0.05, 0.07, or 0.1 mg PO OD)

Follow-Up every 6 month after randomization

Sample size calculation based on estimation
- at initial trial design: n=2190
- after trial extension 2019: n=1653

With funding from the:
Federal Ministry of Research, Technology and Space

Baseline Characteristics I

Well balanced between treatment groups

DIGIT-HF

Characteristic	Digitoxin (N = 613)	Placebo (N = 599)
Age – yr	66.0 ± 11.1	65.8 ± 11.4
Female sex – no. (%)	122 (19.9)	125 (20.9)
NYHA functional class - no. (%)		
II	181 (29.5)	178 (29.7)
III	408 (66.6)	399 (66.6)
IV	24 (3.9)	22 (3.7)
Left ventricular ejection fraction – %	28.4 ± 6.9	28.9 ± 6.7
Main cause of heart failure – no. (%)		
Ischemic	323 (53.1)	310 (52.4)
Non-ischemic/Unknown	285 (46.9)	282 (47.6)
Body mass index – kg/m²	29.3 ± 5.7	28.9 ± 5.6
Heart rate – beats/min	73.7 ± 11.9	74.1 ± 12.3
Systolic blood pressure – mmHg	120.5 ± 18.6	121.4 ± 18.8
Atrial fibrilliation – no. (%)	169 (27.6)	161 (26.9)
Estimated glomerular filtration rate		
Mean – ml/min/1.73 m²	65.0 ± 23.0	65.2 ± 23.7
≤60 ml/min/1.73 m² – no./total no. (%)	263 (43.0)	257 (42.9)

70% NYHA III-IV

With funding from the:
Federal Ministry of Research, Technology and Space

Baseline Characteristics II

Well implemented heart failure therapy

Characteristic	Digitoxin (N = 613)	Placebo (N = 599)
Heart failure medication – no. (%)		
Beta-blocker	593 (96.7)	567 (94.7)
Angiotensin-converting-enzyme inhibitor	222 (36.2)	213 (35.6)
Angiotensin receptor blocker	113 (18.4)	115 (19.2)
Angiotensin receptor-neprilysin inhibitor	248 (40.5)	231 (38.6)
Mineralocorticoid receptor antagonist	466 (76.0)	458 (76.5)
Sodium-glucose cotransporter 2 inhibitor	121 (19.7)	113 (18.9)
Cardiac glycoside	3 (0.5)	6 (1.0)
Device therapy – no. (%)		
Implantable cardioverter-defibrillator therapy	415 (67.7)	364 (60.9)
Cardiac resynchronisation therapy	162 (26.4)	144 (24.1)

BB 95%

RASi 93%

ARNI 40%

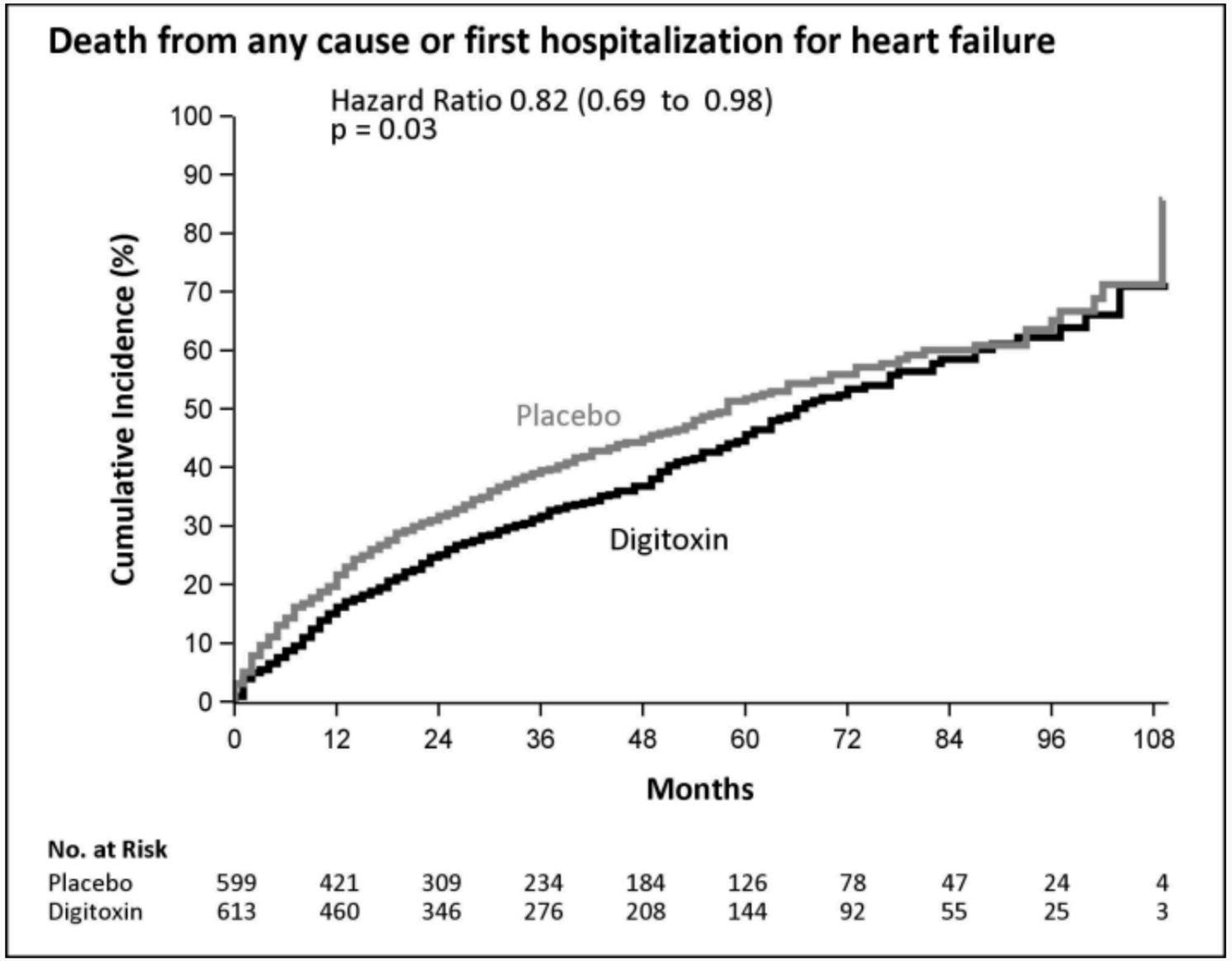
MRA 76%

SGLT2i 19%

ICD 65%

CRT 25%

Primary Outcome



Absolut risk reduction: 4.6%

Number-needed-to-treat: 22

Median time of follow-Up: 36 month

With funding from the:
Federal Ministry of Research, Technology and Space

Take home messages

- **Herzinsuffizienz ist häufig**
- **Diagnostik: NT-proBNP, Echo, ev. MRI**
- **HFrEF/HFmrEF: Entresto (ACEI), SGLT2-Hemmer, MRA, BB, Digitoxin**
- **HFpEF: SGLT2-Hemmer, MRA (Finenerone)**
- **Medikamente rasch auftitrieren, keine Flüssigkeitsrestriktion**
- **EF <35%: ICD erwägen, CRT bei LSB**
- **An Amyloidose denken**

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(Giovanni Trapattoni)

„Ich habe fertig!“

Merci!

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