Maximaliser le traitement médical de l'Insuffisance Cardiaque

Quels bénéfices?

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Heart failure – Terminology related to LVEF

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]

HFrEF → **LVEF ≤ 40%**

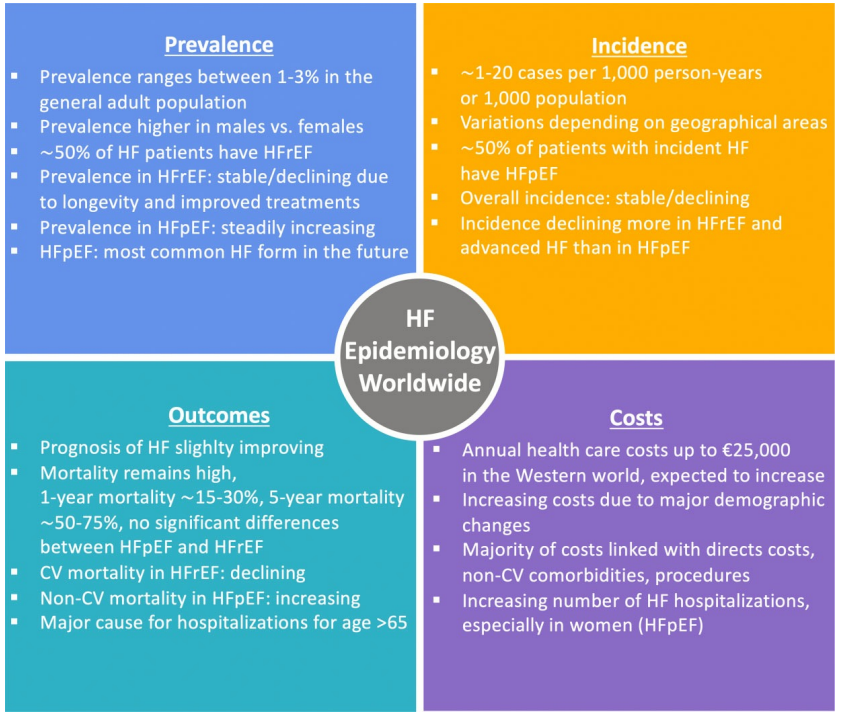
HFmrEF → **LVEF 41 et 49%**

HFpEF → **LVEF ≥ 50%**

McDonagh T, et al. Eur Heart J 2021

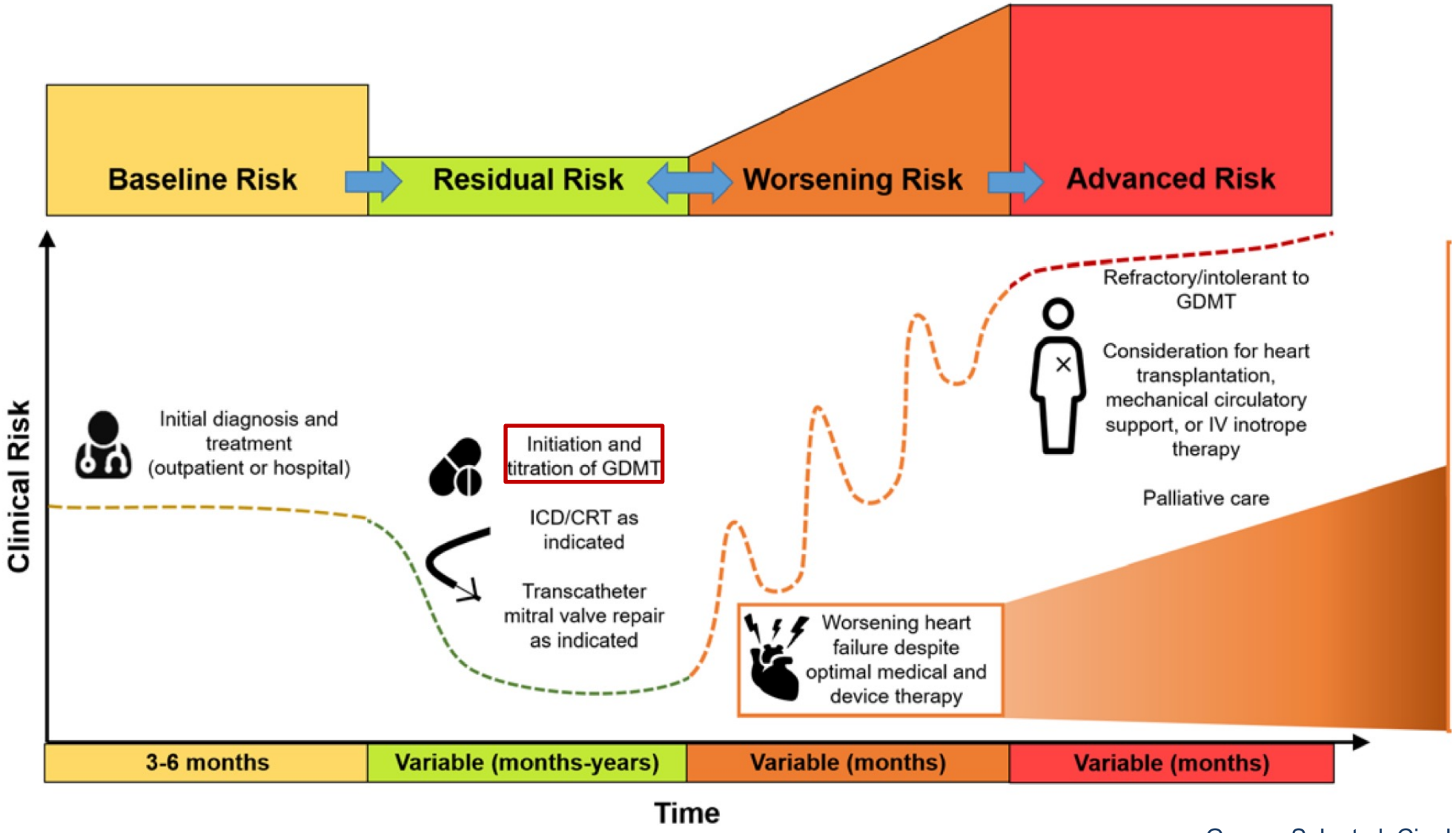
Global epidemiology in heart failure

- 1-3% de la population adulte (250 000 en Belgique): 50% HpEF
- Prevalence in HFpEF steadly increasing: HFpEF most common form of HF in the future
- 50% of incident HF have HFpEF
- Mortality remains high
- CV mortality in HFrEF declining
- Non-CV mortality in HFpEF increasing
- Major cause for hospitalisations for age > 65y
- Increasing number of HF hospitalisations in women (HFpEF)



Becher PM, et al. Eur Heart J (2022) 43, 3005–3007

Risk profiles for chronic heart failure over time



Greene S.J. et al. Circ Heart Fail. 2020

Increased mortality due to hospitalisation for HF

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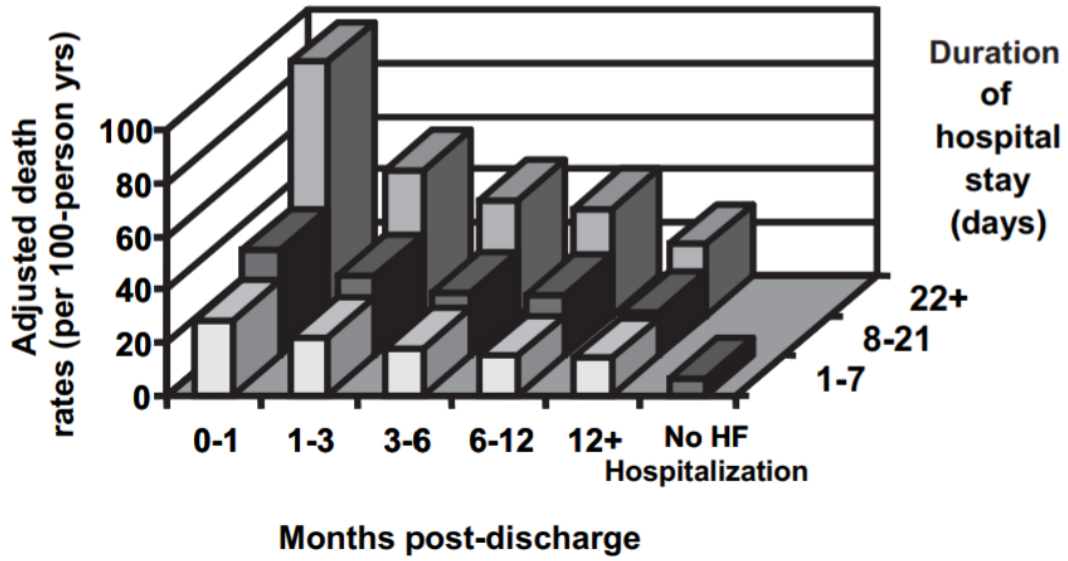
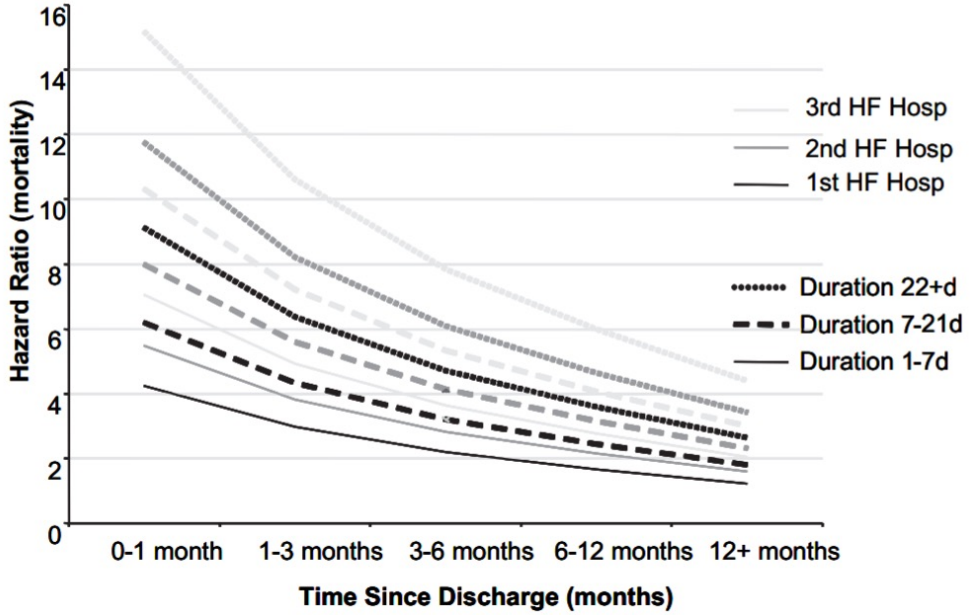
Higher risk for mortality

- Shortly after hospitalization
- With increased number of hospitalizations
- With increased duration of hospitalization





Solomon SD, et al. Circulation. 2007. PMID: 17724259;
Hollenberg S et al. J Am Coll Cardiol 2019;74:1966–2011

Pharmacological treatments for patients with Heart Failure with Reduced Ejection fraction (HFrEF)

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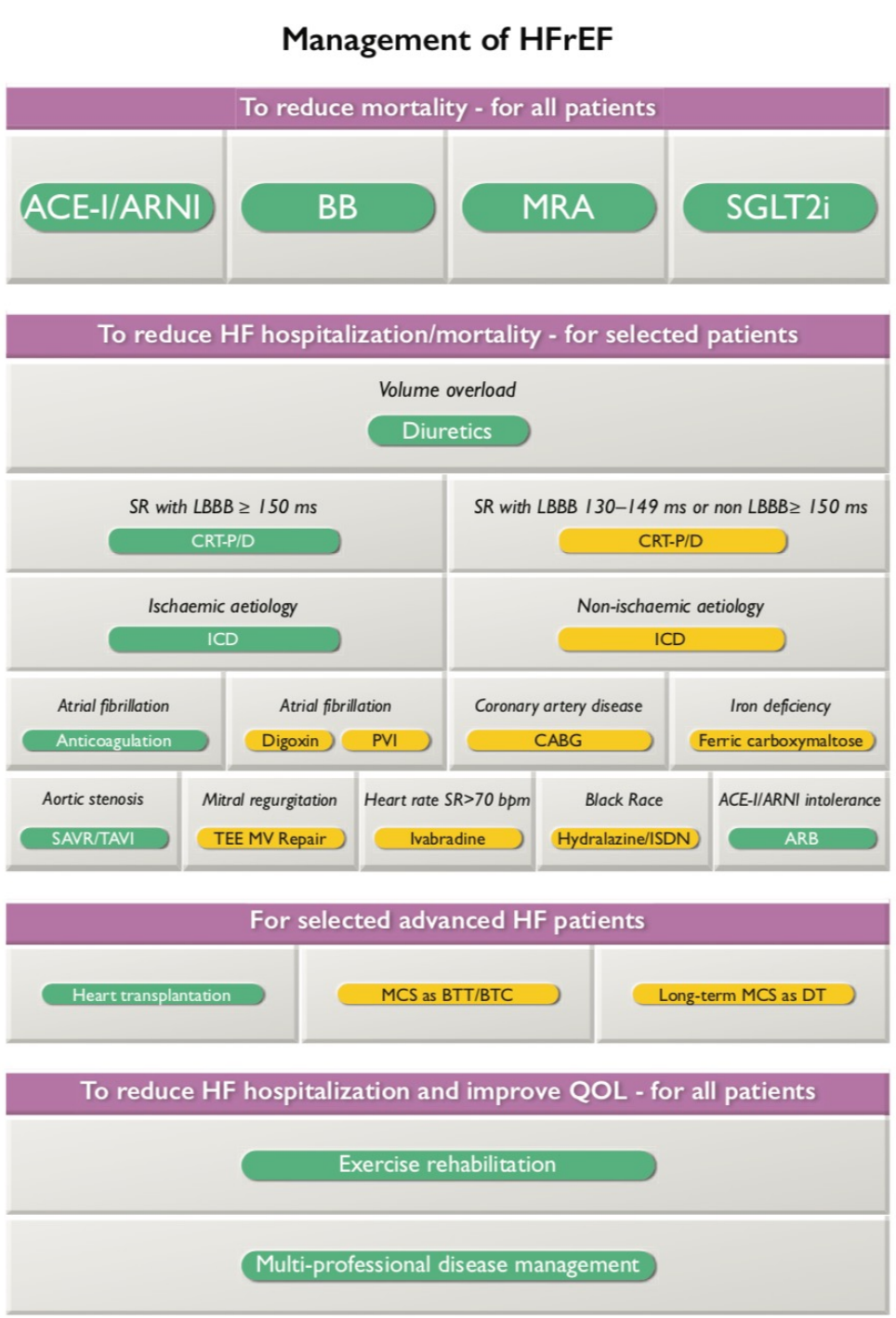
The goals of pharmacotherapy in patients with HFrEF are:

- Reduce mortality
- Prevent recurrent hospitalizations due to worsening HF
- improve their clinical status, functional capacity and quality of life

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]

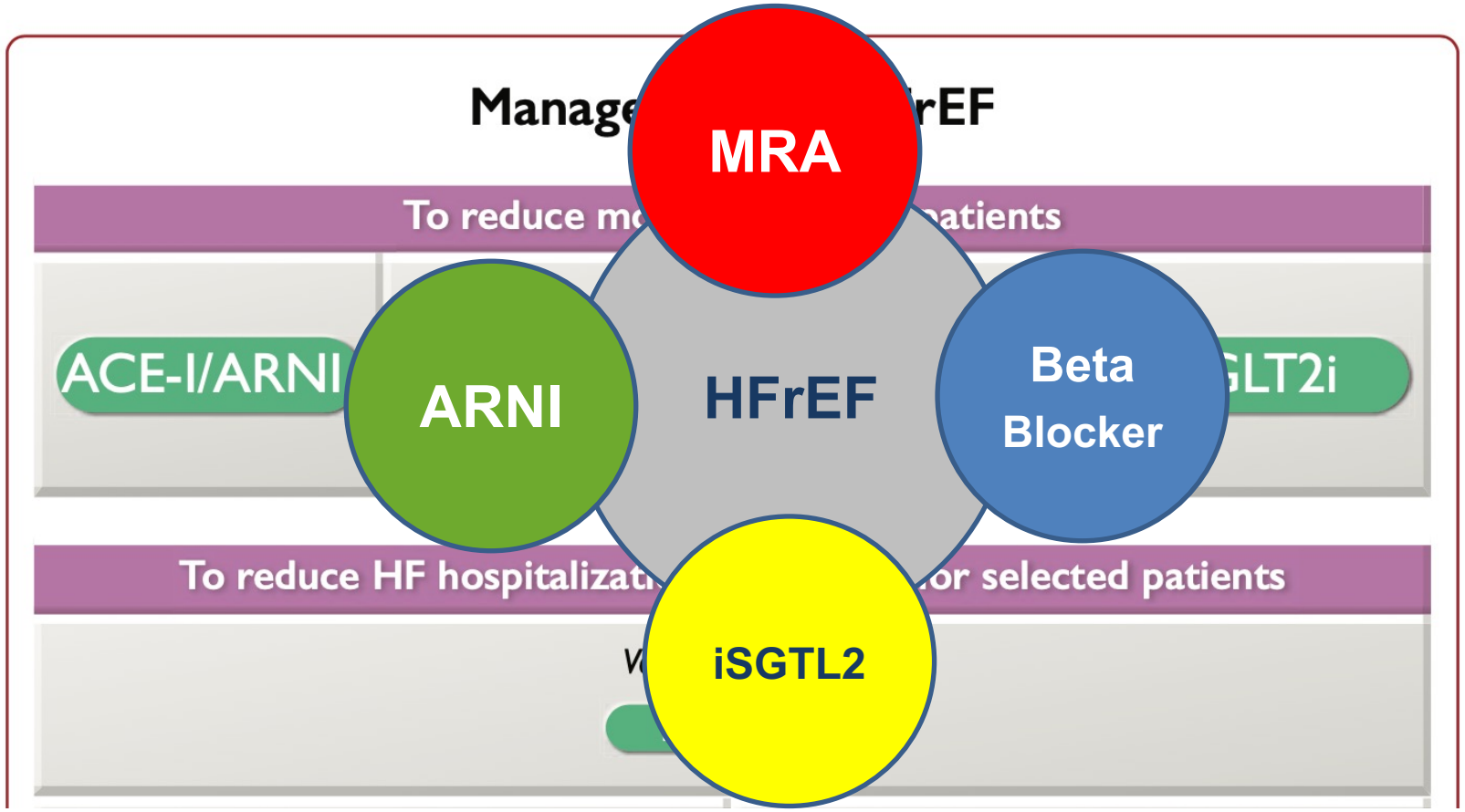
McDonagh T, et al. Eur Heart J 2021

Treatment HFrEF



McDonagh T, et al. Eur Heart J 2021;00:1-128

HF Treatment according to LVEF
HFrEF (≤ 40%)



- Quick introduction
- Quick titration
- No sequential order

McDonagh T, et al. Eur Heart J 2021

Pharmacological treatments for patients with Heart Failure with Reduced Ejection fraction (HFrEF)

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In all patients

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

In selected patients

Other agents		
Candesartan	4 mg *o.d.*	32 mg *o.d.*
Losartan	50 mg *o.d.*	150 mg *o.d.*
Valsartan	40 mg *b.i.d.*	160 mg *b.i.d.*
Ivabradine	5 mg *b.i.d.*	7.5 mg *b.i.d.*
Vericiguat	2.5 mg *o.d.*	10 mg *o.d.*
Digoxin	62.5 µg *o.d.*	250 µg *o.d.*
Hydralazine/ Isosorbide dinitrate	37.5 mg *t.i.d.*/20 mg *t.i.d.*	75 mg *t.i.d.*/40 mg *t.i.d.*

	Starting dose	Target dose
ACE-I		
Captopril[a]	6.25 mg *t.i.d.*	50 mg *t.i.d.*
Enalapril	2.5 mg *b.i.d.*	10–20 mg *b.i.d.*
Lisinopril[b]	2.5–5 mg *o.d.*	20–35 mg *o.d.*
Ramipril	2.5 mg *b.i.d.*	5 mg *b.i.d.*
Trandolapril[a]	0.5 mg *o.d.*	4 mg *o.d.*
ARNI		
Sacubitril/valsartan	49/51 mg *b.i.d.*[c]	97/103 mg *b.i.d.*
Beta-blockers		
Bisoprolol	1.25 mg *o.d.*	10 mg *o.d.*
Carvedilol	3.125 mg *b.i.d.*	25 mg *b.i.d.*[e]
Metoprolol succinate (CR/XL)	12.5–25 mg *o.d.*	200 mg *o.d.*
Nebivolol[d]	1.25 mg *o.d.*	10 mg *o.d.*
MRA		
Eplerenone	25 mg *o.d.*	50 mg *o.d.*
Spironolactone	25 mg *o.d.*[f]	50 mg *o.d.*
SGLT2 inhibitor		
Dapagliflozin	10 mg *o.d.*	10 mg *o.d.*
Empagliflozin	10 mg *o.d.*	10 mg *o.d.*

McDonagh T, et al. Eur Heart J 2021;00:1-128

Angiotensin–Neprilysin Inhibition vs Enalapril in HF
PARADIGM-HF

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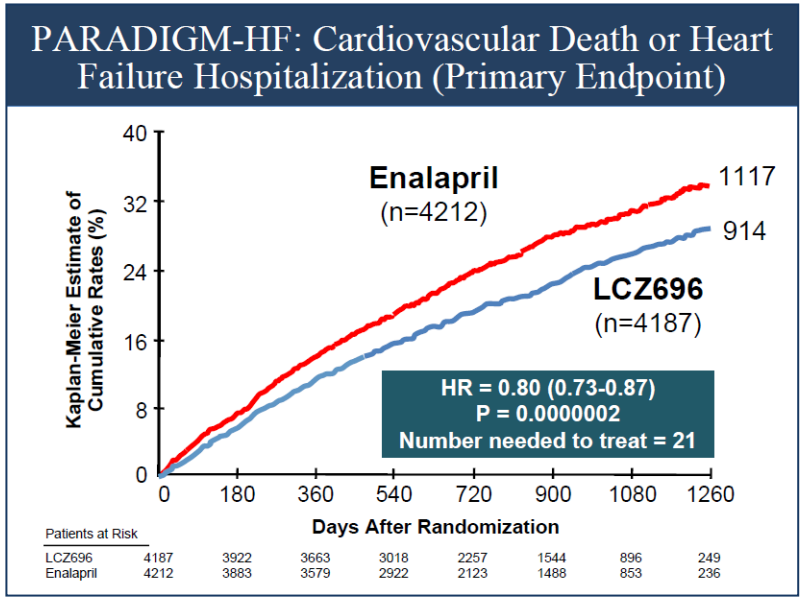
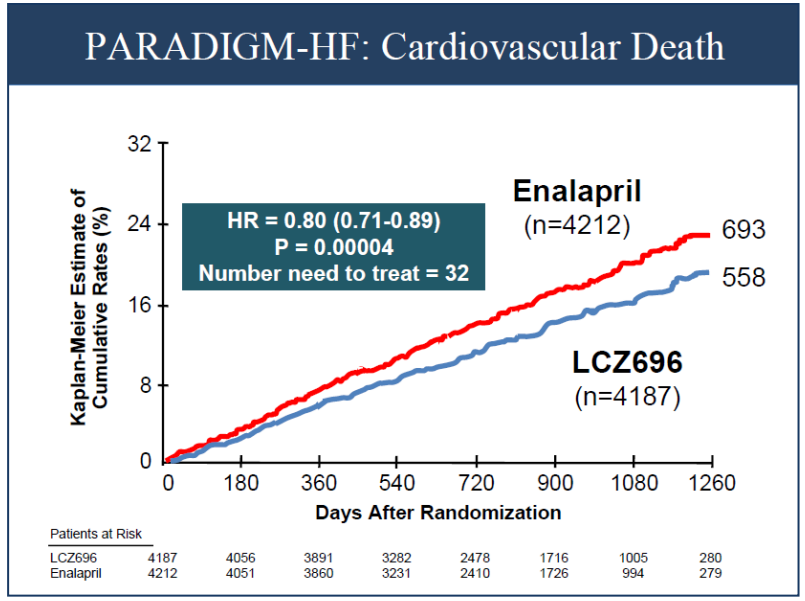
I B

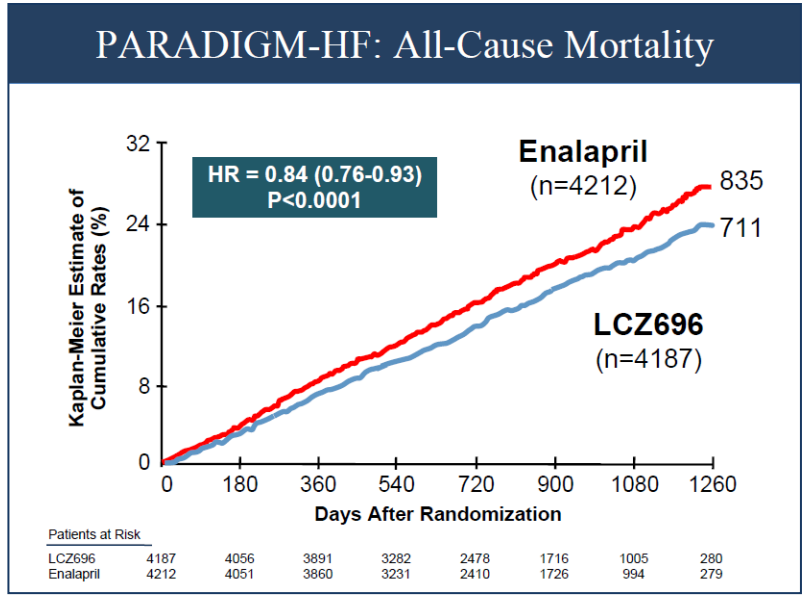
- Reduce the degradation of BNP, enhacing diuresis, natriuresis, myocardial relaxation
- Inhibit renin and aldosterone secretion

↓ CV death and
↓ hospitalisation for worsening HF

- **N = 8442 patients**
- **EF ≤ 40%**
- **SV x Enalapril**
- **Primary EP:** composite of CV death and hospitalisation for worsening HF



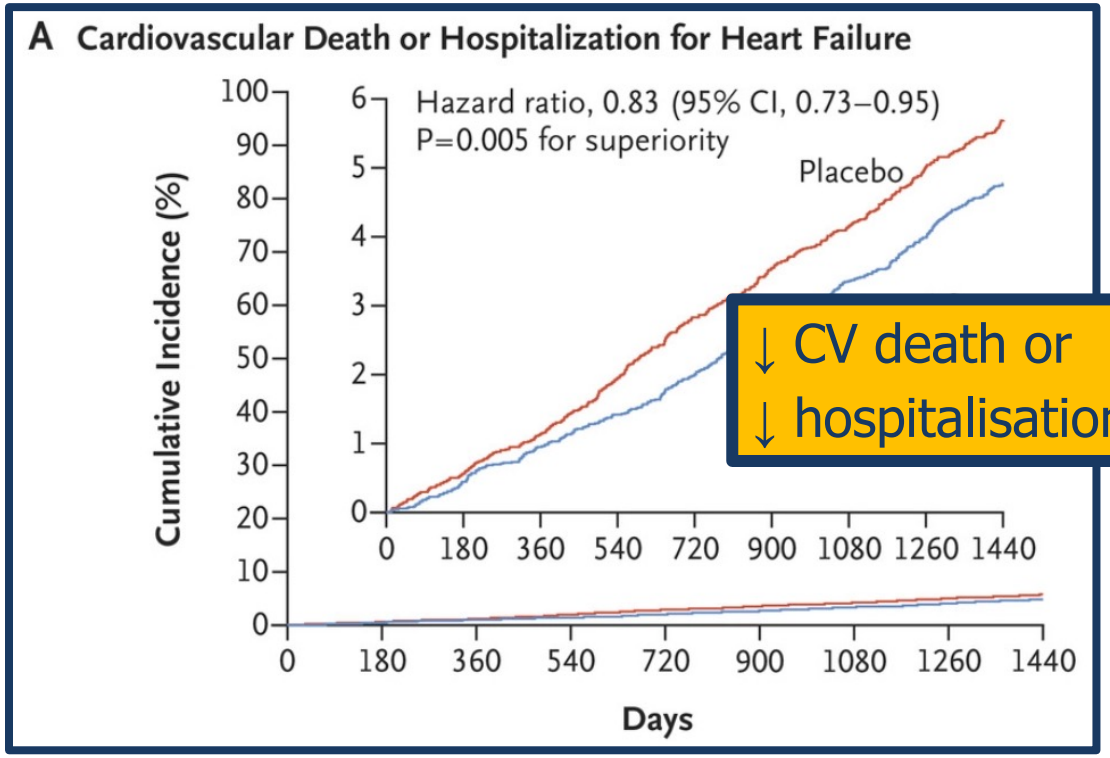




McMurray JJ et al. N Engl J Med 2014;371:993-1004

Sodium-glucose co-transporter 2 inhibitors - iSGTL2

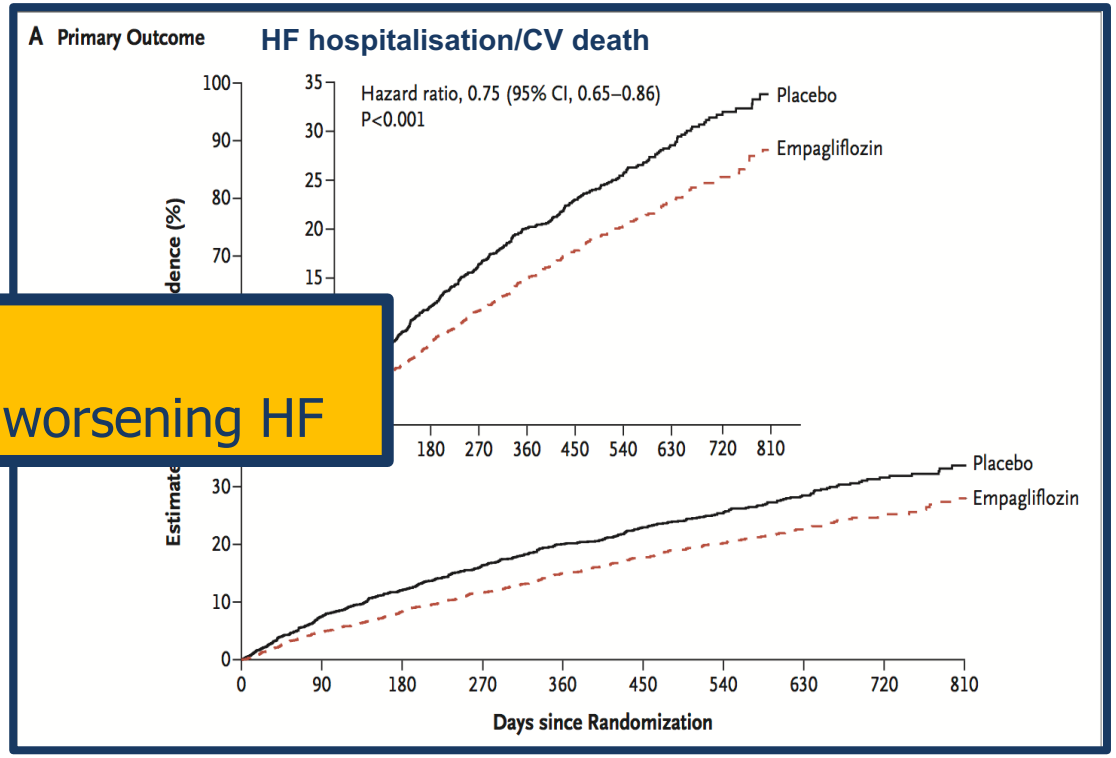
DAPA-HF (Dapagliflozin)



Wiviott et al. N Engl J Med 2019

- **N = 4744 patients**
- **EF ≤ 40%**
- **Dapagliflozin or placebo**
- **Primary EP:** HF hospitalisation/urgent visit, CV death

EMPEROR-Reduced Trial (Empagliflozin)

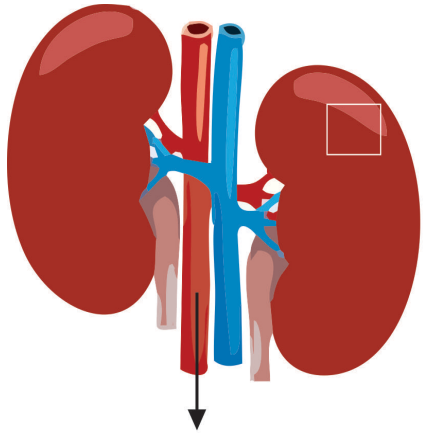


Packer et al, N Engl J Med 2020

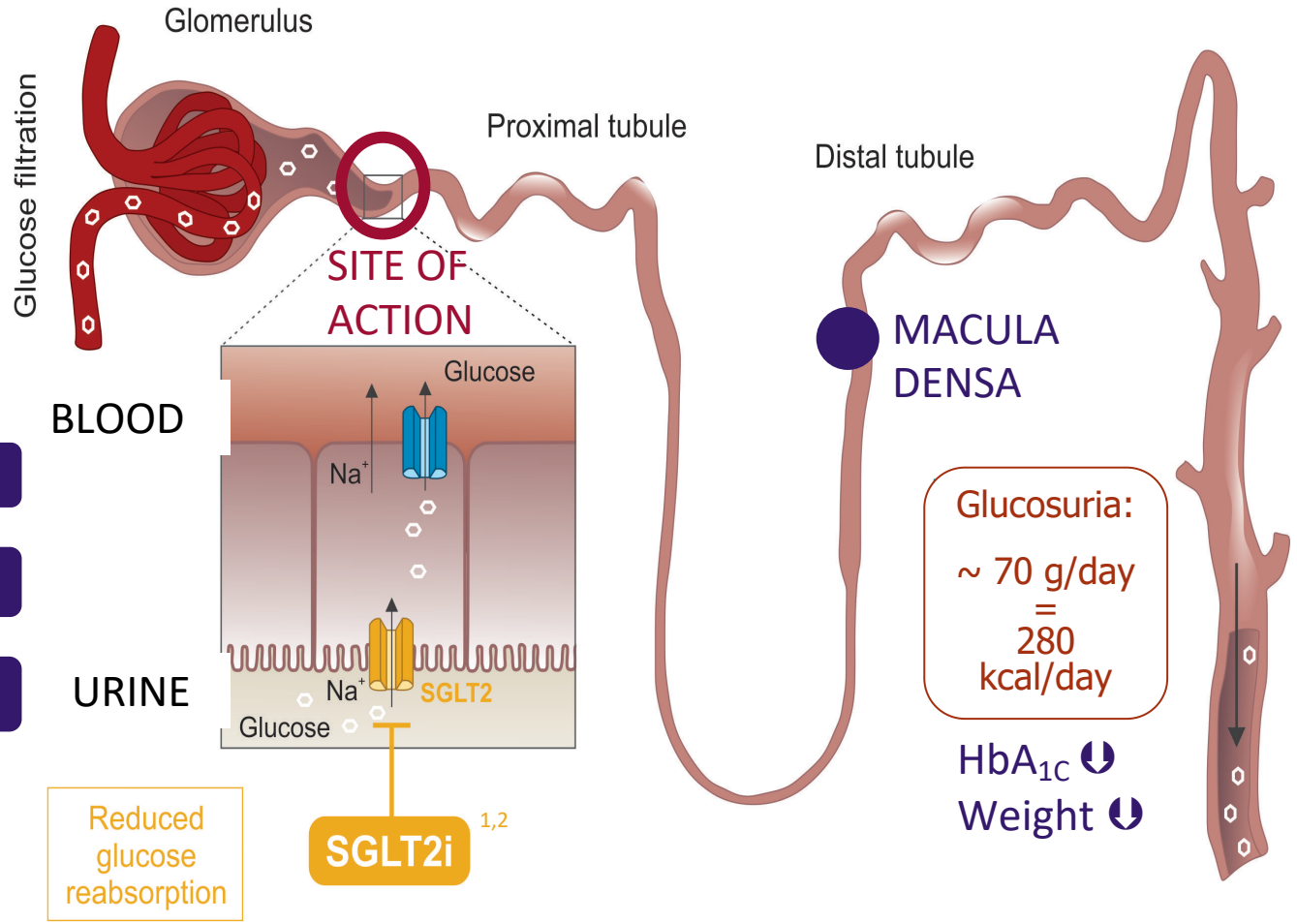
↓ CV death or
↓ hospitalisation for worsening HF

- **N = 3730 patients**
- **EF ≤ 40%**
- **Empagliflozin or placebo**
- **Primary EP: composite:** HF hospitalisation/CV death

Sodium-glucose co-transporter 2 inhibitors - iSGTL2



- GLUCOSURIA[5]
- NATRIURESIS[3,4]
- OSMOTIC DIURESIS[3,4]



SLGT2i
Protection cardiaque et rénale

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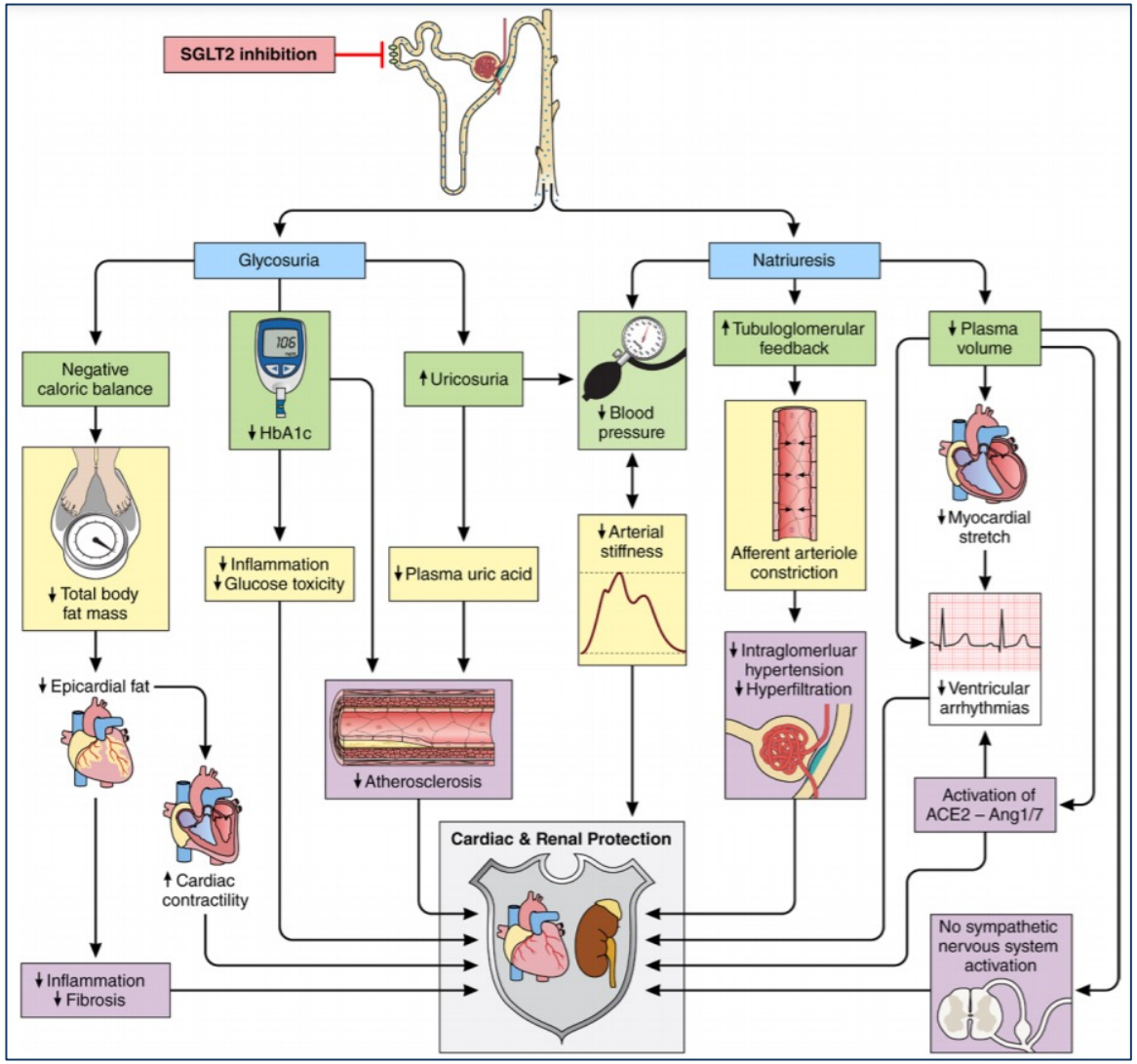
1. Glycosuria

- Decreased inflammation and glucotoxicity
- Weight loss decreasing epicardial fat
- Uricosuria with beneficial effect on atherosclerosis
- Improving myocardial energetics (ketonbodies)

2. Natriuresis

- Lowering blood pressure and improving endothelial function
- Restoring the tubuloglomerular feedback and reducing hyperfiltration
- Lowering plasma volume and congestion



Heerspink et al. Circulation 2016

Guideline recommended therapy in HFrEF
Impact on mortality

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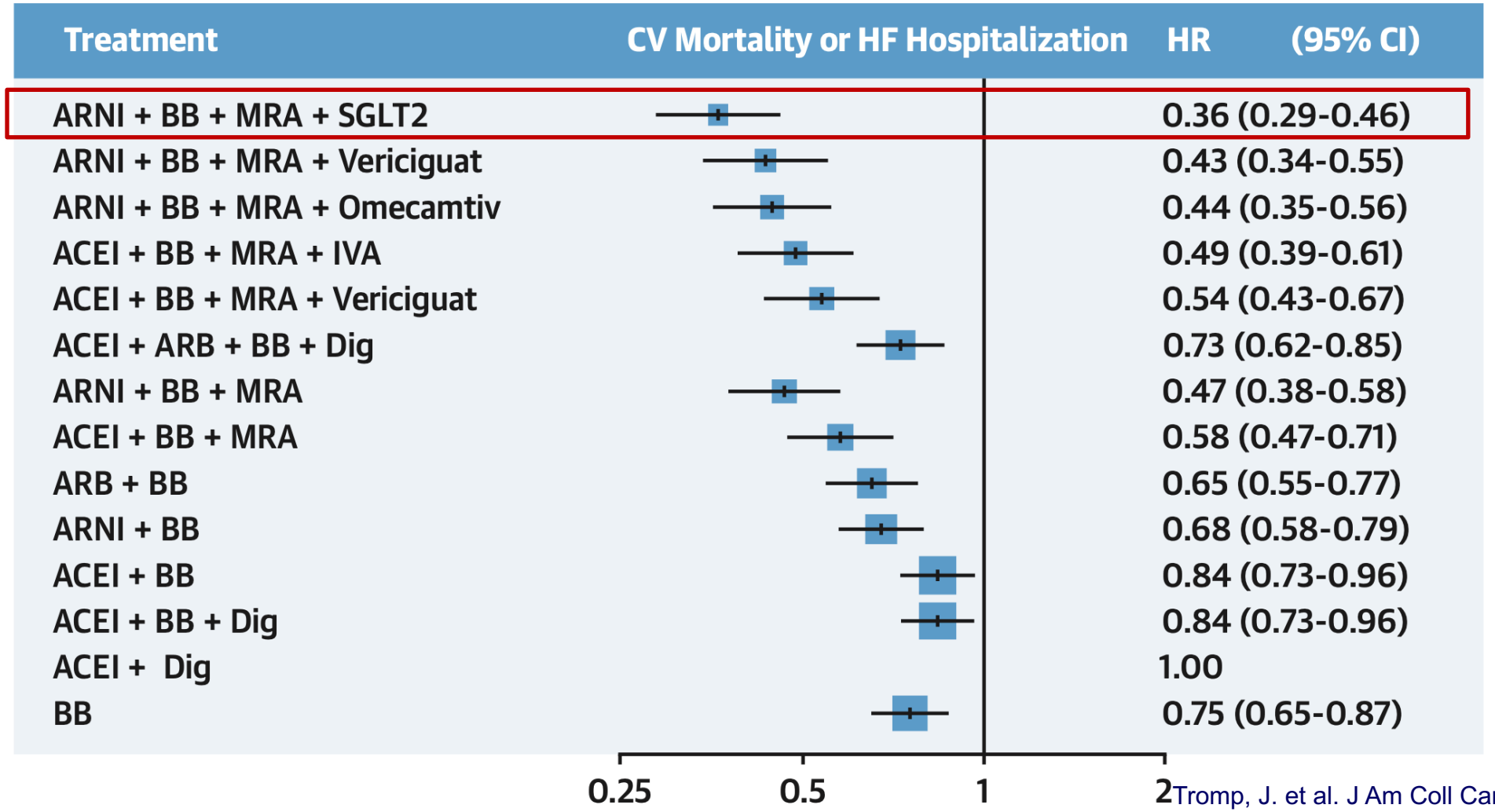
Network meta-analysis for all-cause mortality:
Study drug vs placebo



Tromp, J. et al. J Am Coll Cardiol HF. 2022;10(2):73–84.

Titration of guideline recommended therapy
Impact on mortality

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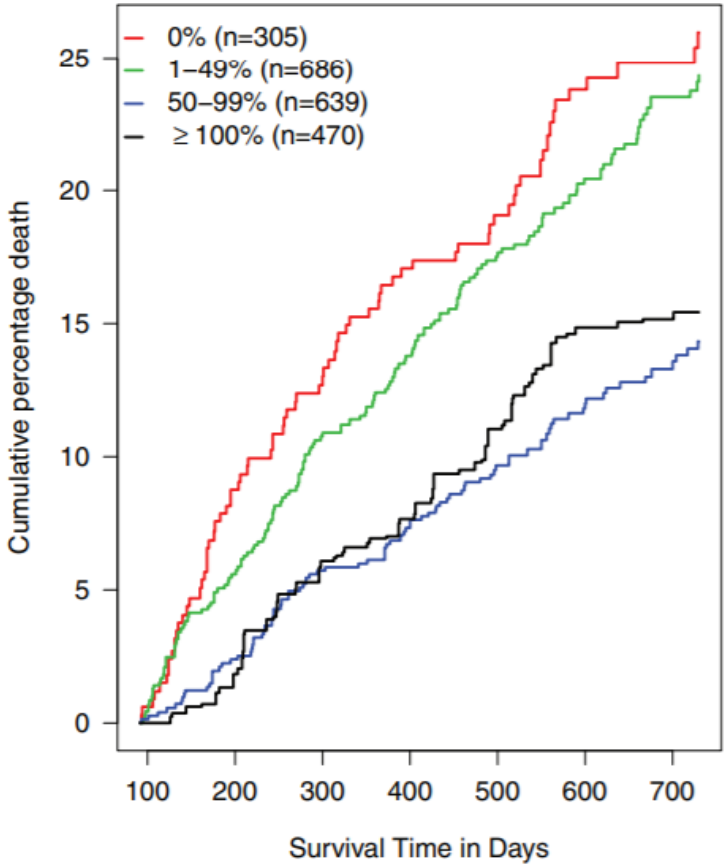
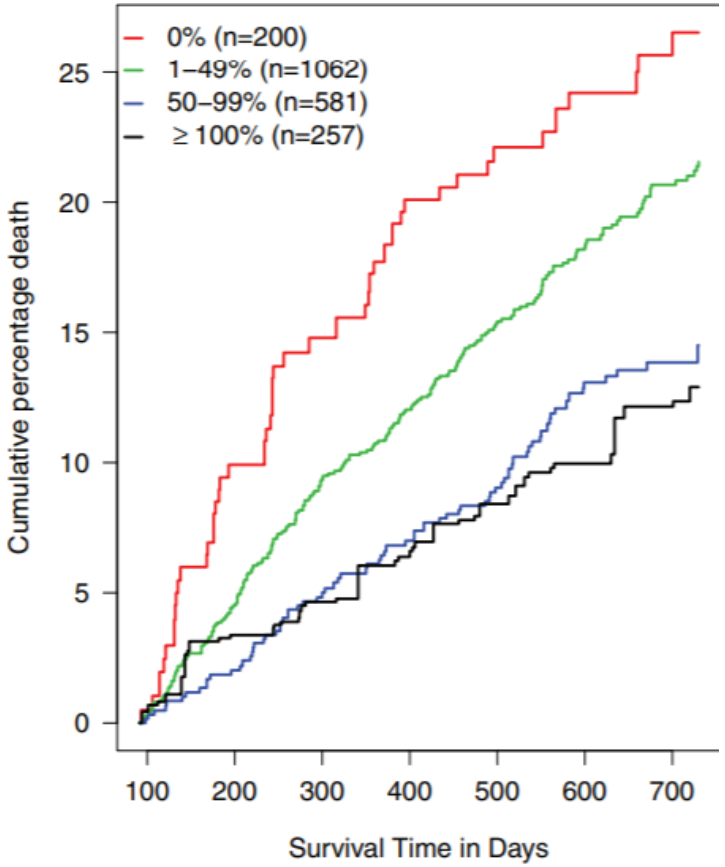
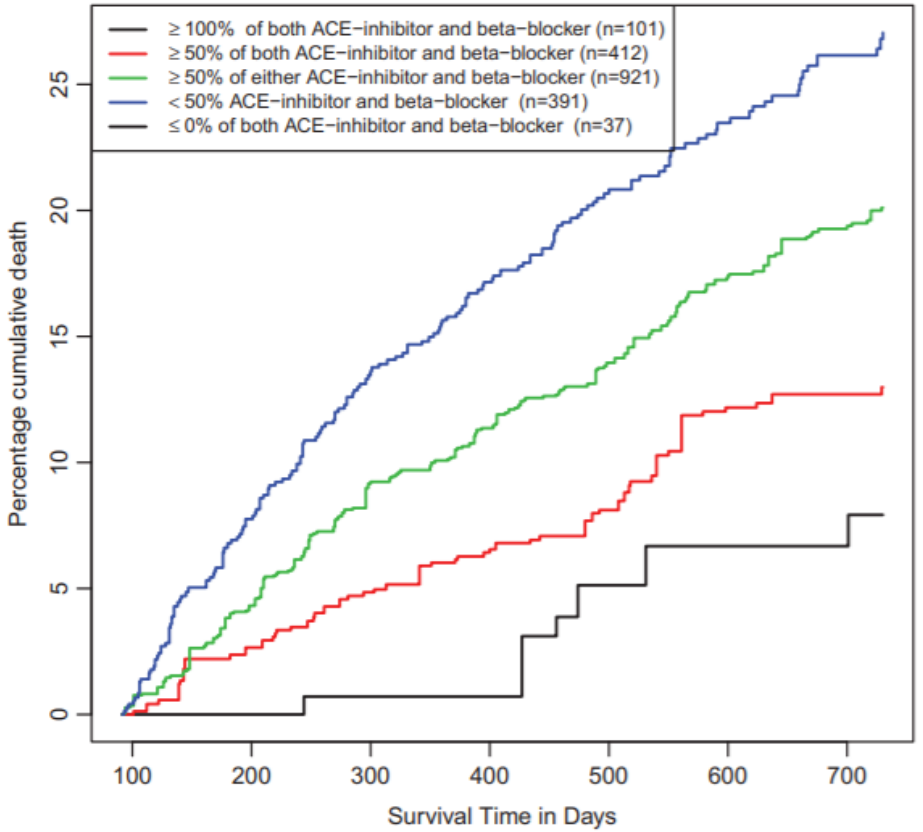
ACEinhibitor/ARB



Betablocker



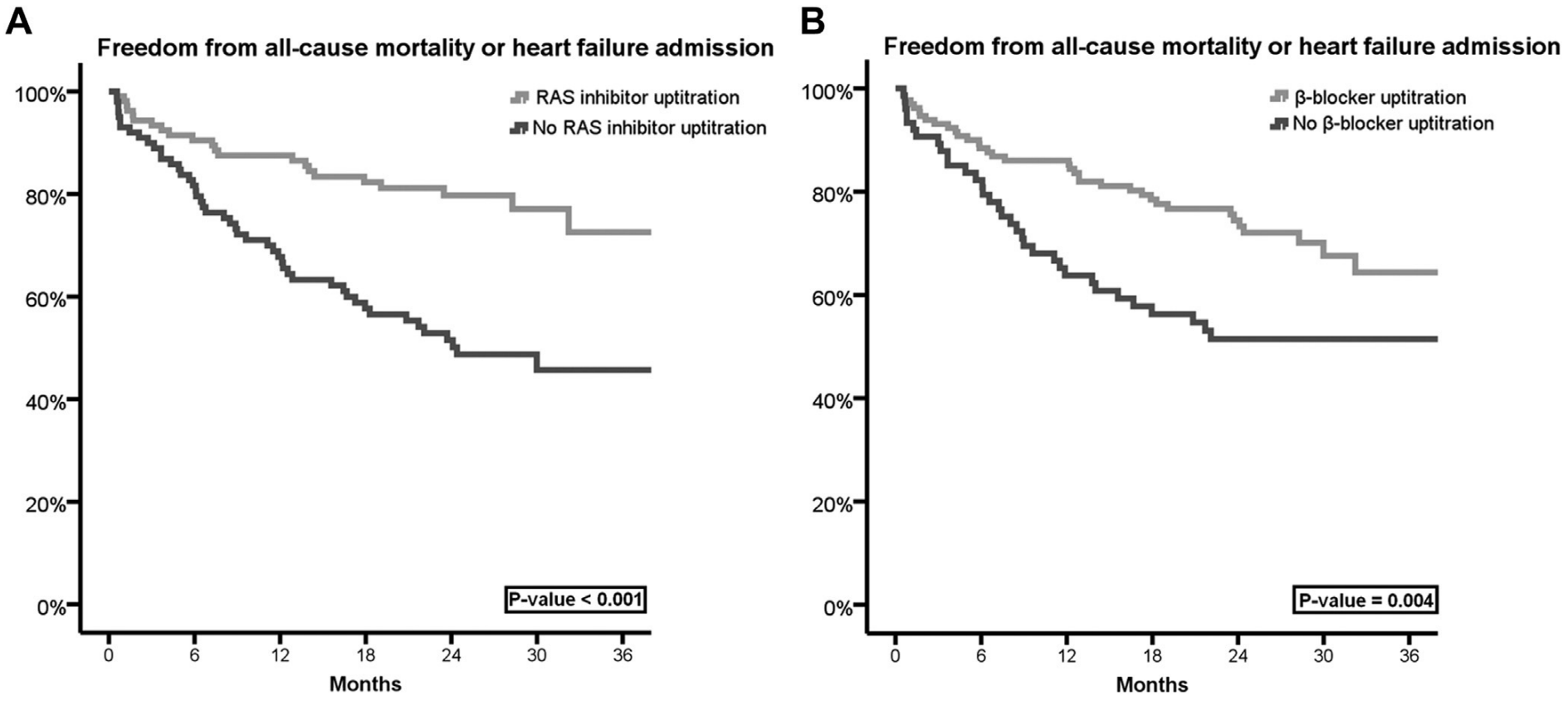
Combination



Ouwerkerk et al. Eur. Heart. J. 2017 Jun 21;38(24):1883-1890

Titration of guideline recommended therapy
Impact on outcome

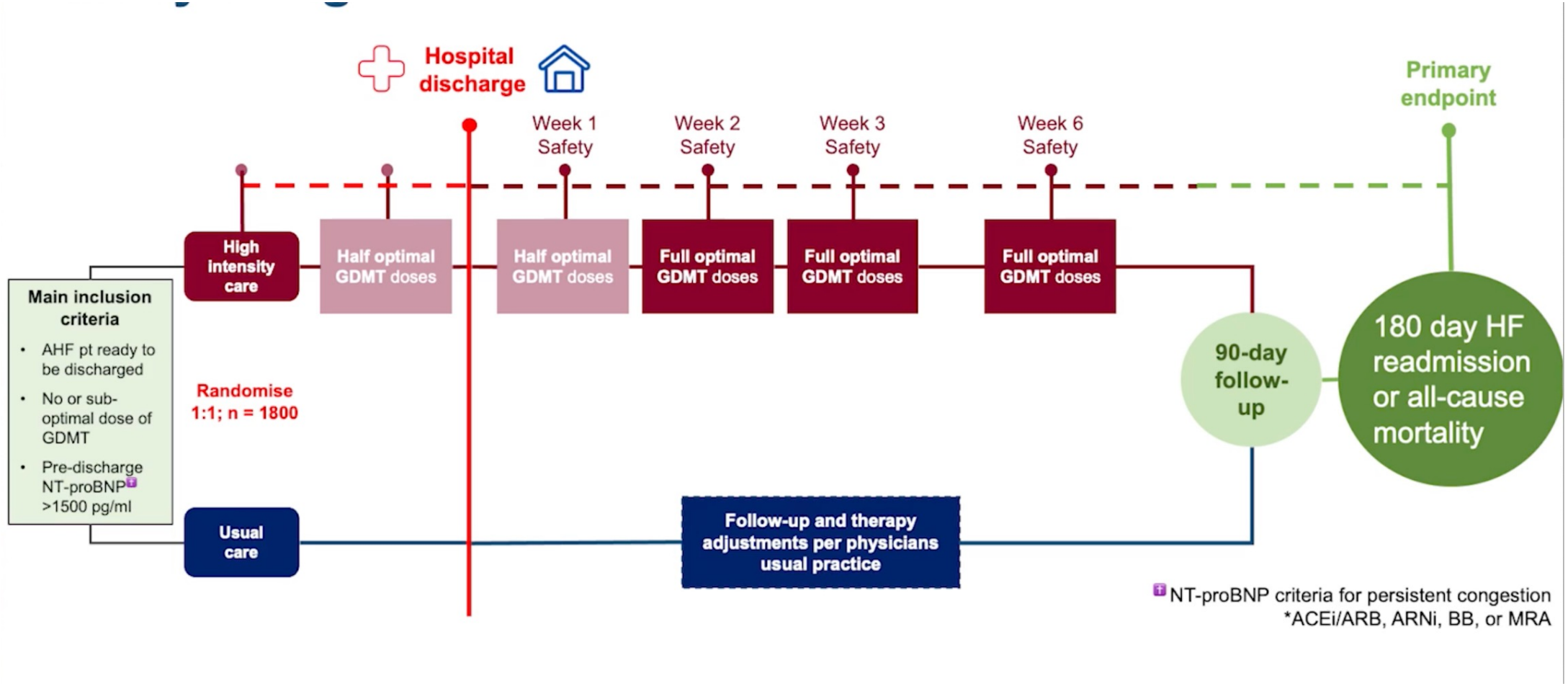
- N=209 consecutive patients with EF < 40%, after discharge and at follow up



Verbrugge H et al. Am J Cardiol 2013;112:1913e1920

STRONG-HF trial

Study design

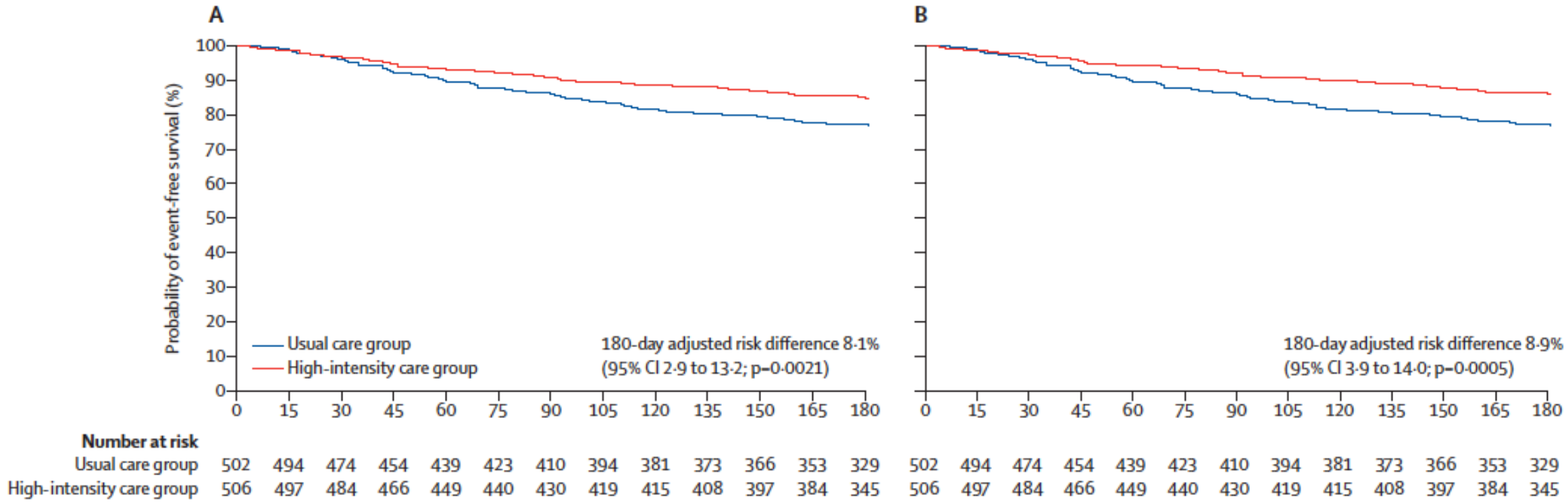


Mebazaa A et al. Lancet 2022

STRONG-HF trial

Primary endpoint

↓ HF readmission or all-cause mortality at 180 days



Mebazaa A et al. Lancet 2022

Use of guideline recommended therapy
In real life daily practice

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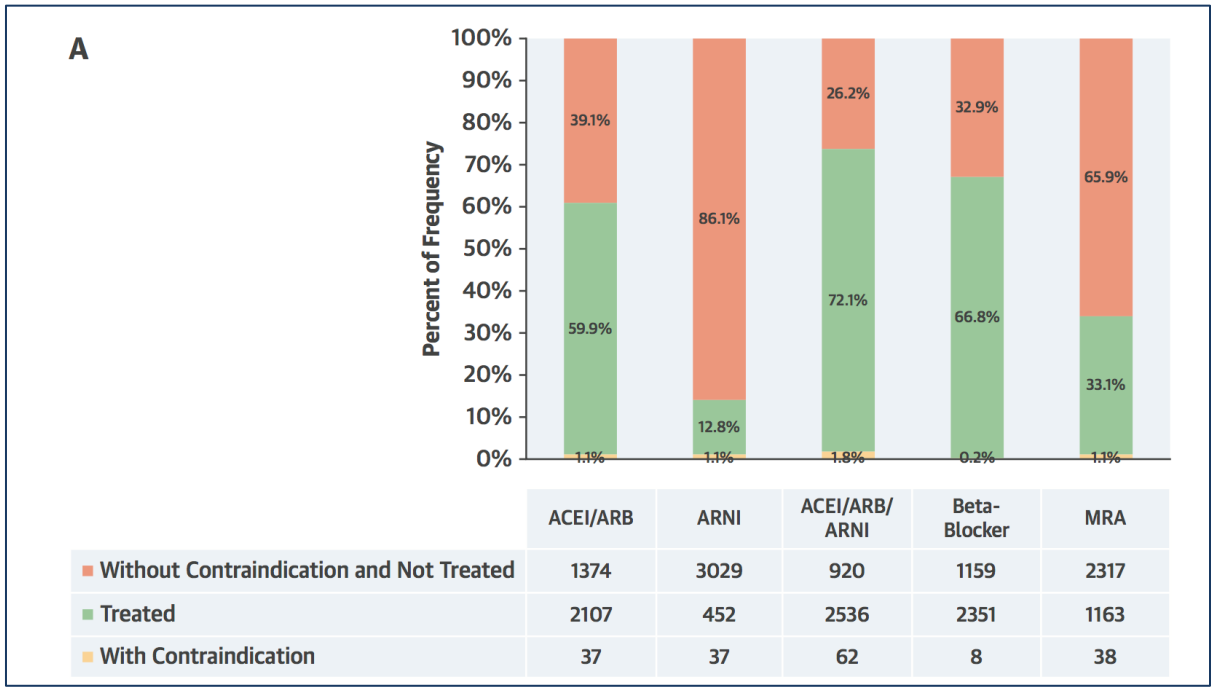
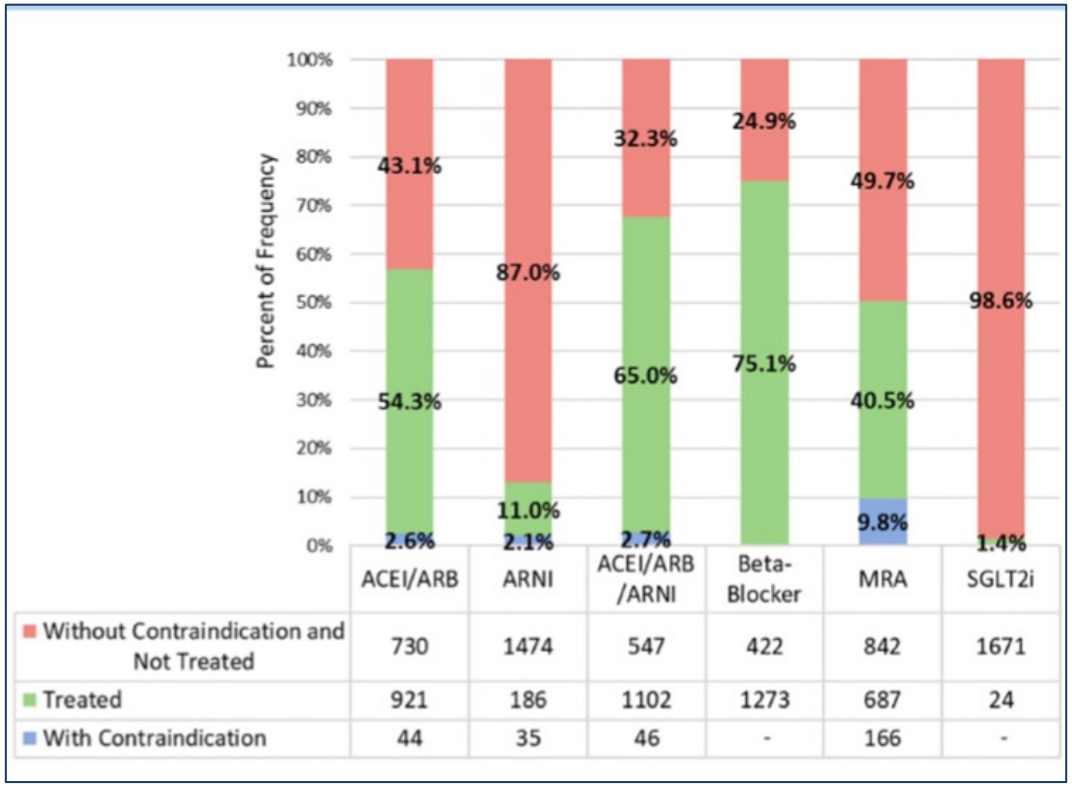
GDMT Patients With Chronic HFrEF
(3518 HFrEF patients)



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351–66.

GDMT at discharge after hospitalisation in HFrEF patients
(1695 HFrEF patients)

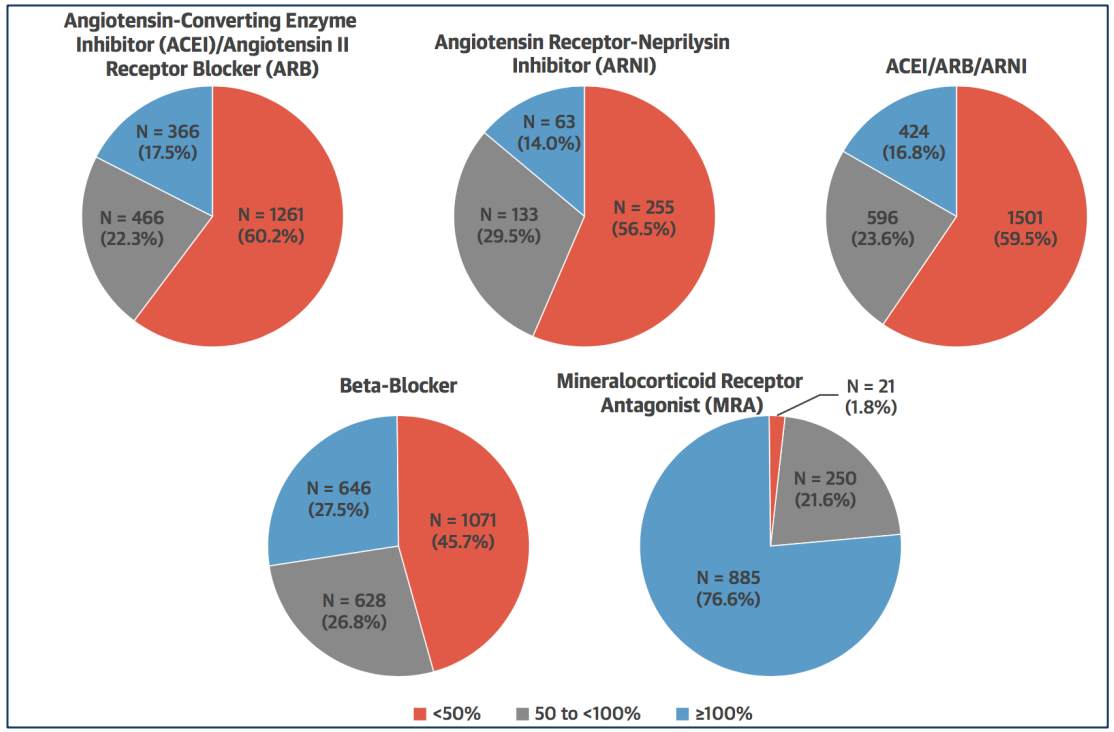


	ACEI/ARB	ARNI	ACEI/ARB /ARNI	Beta-Blocker	MRA	SGLT2i
Without Contraindication and Not Treated	730	1474	547	422	842	1671
Treated	921	186	1102	1273	687	24
With Contraindication	44	35	46	-	166	-

Greene, S.J. et al. J Cardiac Fail 2022;28:10631077

Titration of guideline recommended therapy
In real life daily practice

GDMT Patients With Chronic HFrEF
(3518 HFrEF patients)



Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351–66.

GDMT at discharge after hospitalisation in HFrEF patients
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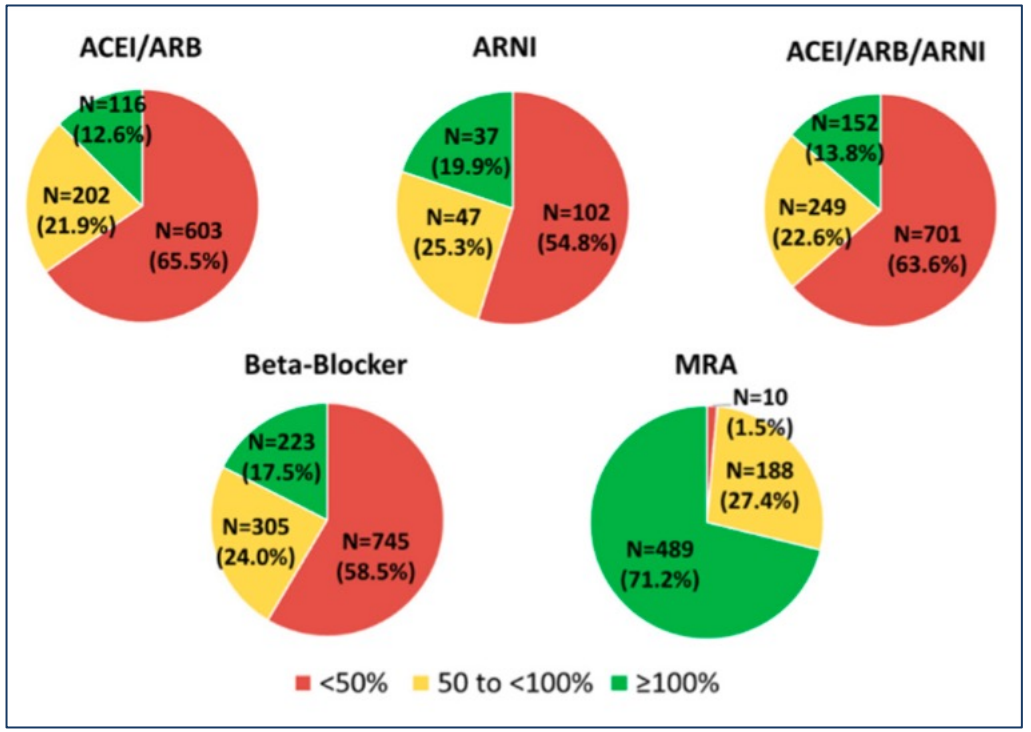
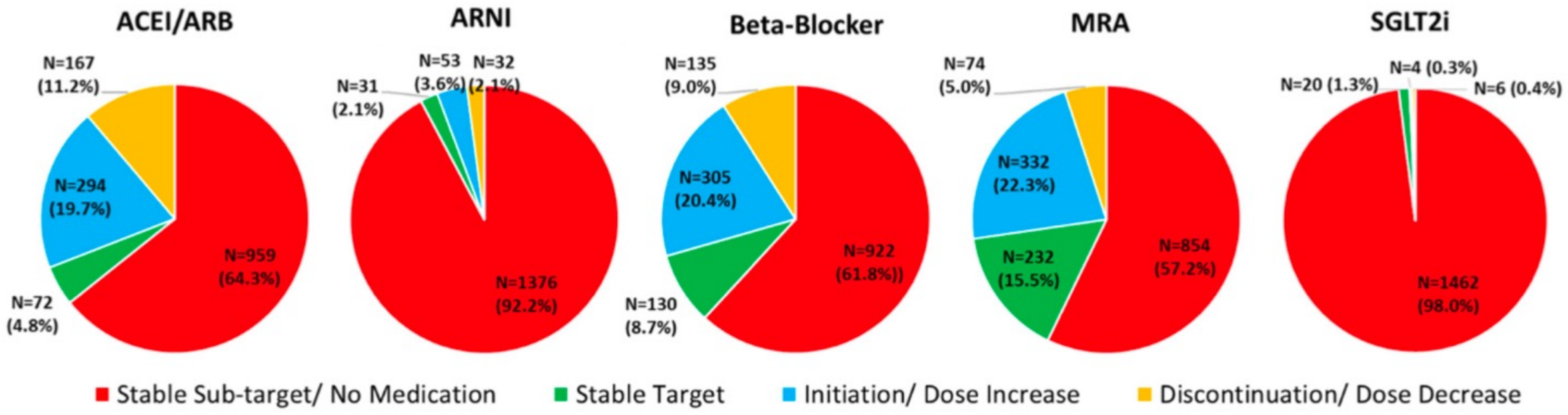


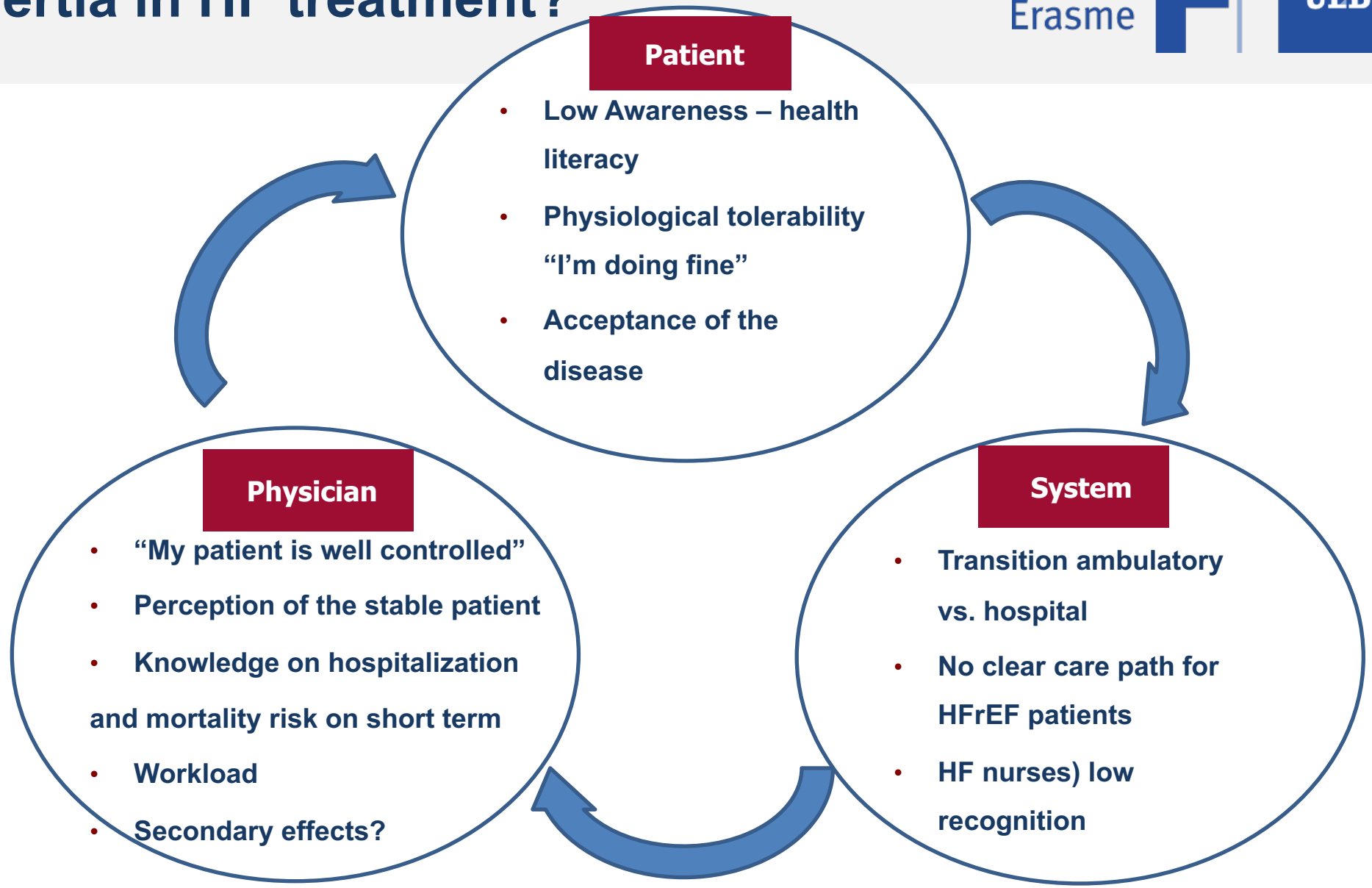
Greene, S.J. et al. J Cardiac Fail 2022;28:10631077

Dose of guideline recommended therapy
At discharge compared to admission



Greene, S.J. et al. J Cardiac Fail 2022;28:10631077

Why inertia in HF treatment?



Bress et al. J Am Coll Cardiol. 2019
Verhestraeten et al. Heart Fail. Rev. 2020

Traitement HFrEF– Pratique clinique

Hypotension

- Symptomatique?
- Tt de l'IC est le seul responsable de l'hypotension?
- Fièvre? Tr digestifs?
- Traitements non nécessaires pour l'IC à FEVG réduite ?
- Besoin en diurétiques?

- Diminution/arrêt diurétiques
- Répartition du traitement dans la journée
- Si les symptômes d'hypotension persistent, ↓ du traitement
- Revalidation Cardiaque

Insuffisance rénale

Augmente la mortalité toute cause

Introduction RAASi et iSGTL2

- Baisse attendue DFG
- ↓ mortalité malgré la ↓ DFG

Arrêt temporaire RAASi :

- ↑ Cr >100% ou >3.5 mg/dL
- DFG <20 mL/min/1.73 m2
- *K^+> 5.5 mEq/L*

Maintenir RAASi dose:

- ↑ Cr < 50% (<3 mg/dL),
- DFG >25 mL/min/1.73 m2.
- ↑ K^+ ≤5.5 mmol/L

Hyperkaliémie

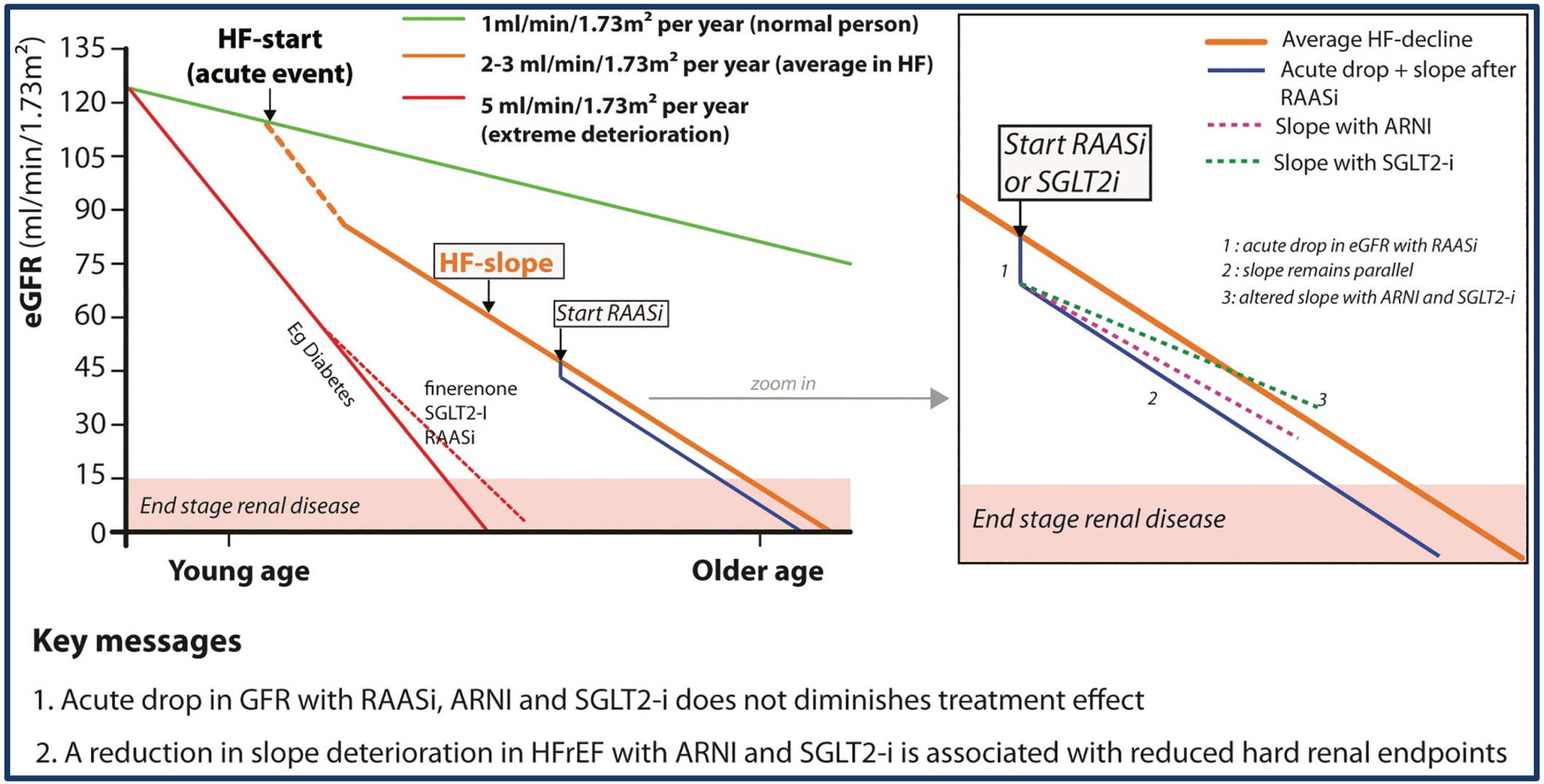
- Hyperkalemia ↑ risque d'arrythmie
- RAASi ↑ risque d'hyperkaliémie

- Si K^+ >5.0 pendant la titration ou sous traitement optimal
- Catium-exchange resins
- K+ binders: patiromer, sodium zirconium cyclocilicate

McDonagh T, et al. Eur Heart J 2021
Cautela J et al. Eur J Heart Failure 2020
Rosano G et al. Eur Heart J – Cardiov Pharmacotherapy 2018

Chronic kidney disease (CKD) and HF

Effect of GDMT on renal slope



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, et al. Eur J Heart Fail 2022

In-hospital initiation and uptitration of quadruple medical therapy HFrEF

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In-Hospital Initiation of Quadruple Medical Therapy for HFrEF

Hospitalized → **Post-Discharge**

	Day 1-4	Days 7-14	Days 14-28	Days 21-42	Beyond
ARNI	Continue	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated	• Maintenance / further optimization of quadruple therapy • Consideration of EP device therapies/ Mitraclip • Consideration of add-on medical therapies or advanced therapies, if refractory • Manage comorbidities
Beta-blocker	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated	Titrate, as tolerated	
MRA	Continue	Titrate, as tolerated	Titrate, as tolerated	Continue	
SGLT2i	Continue	Continue	Continue	Continue	
	Low starting doses Prioritize beta-blocker titration	Benefits of each Rx demonstrated within 30 days of initiation Cumulative benefits within 30 days (>75% relative risk reduction)			Focus on complete set of quadruple medical therapies being implemented

In-Hospital Initiation

More likely to be treated

More likely to tolerate

More likely to fill prescription

More likely to adhere

More likely to persist

More likely to feel better

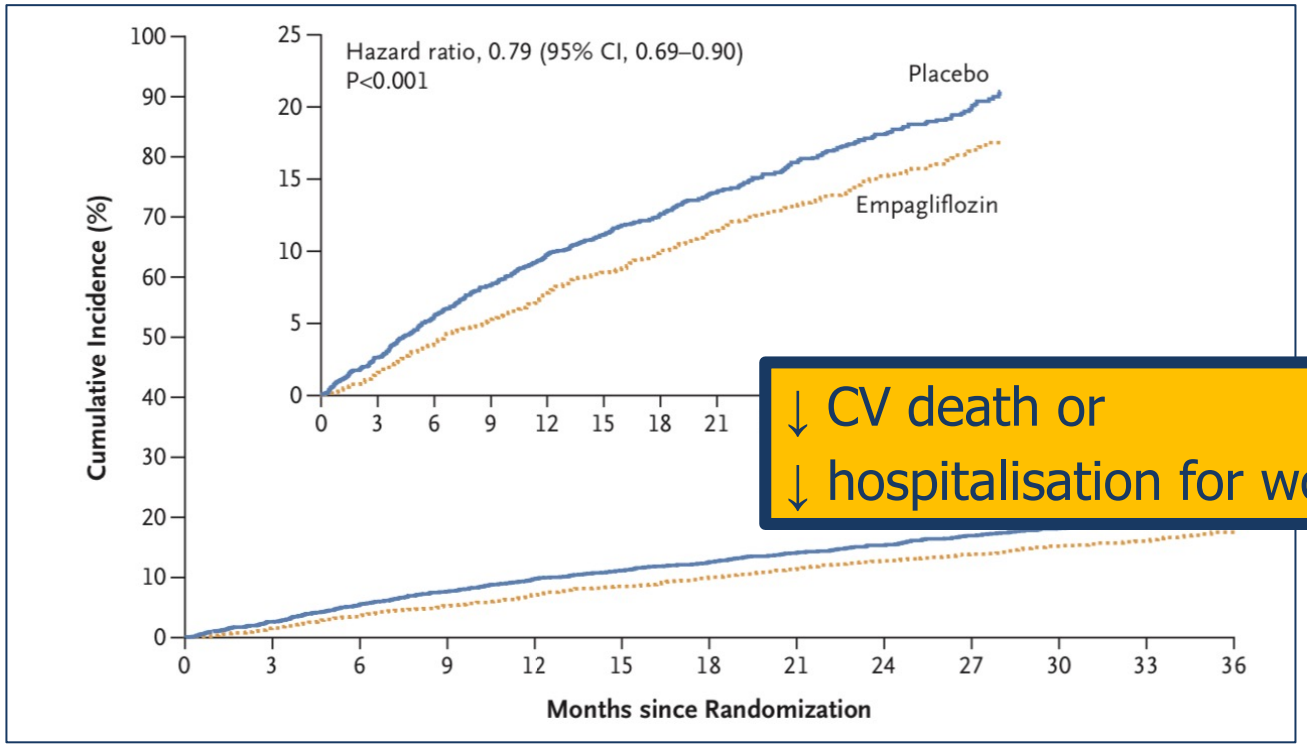
More likely to be home

More likely to survive

Greene SJ, et al. Eur J Heart Fail 2022; 24: 227–229

iSGTL2 in HF with not reduced EF

EMPEROR-PRESERVED trial

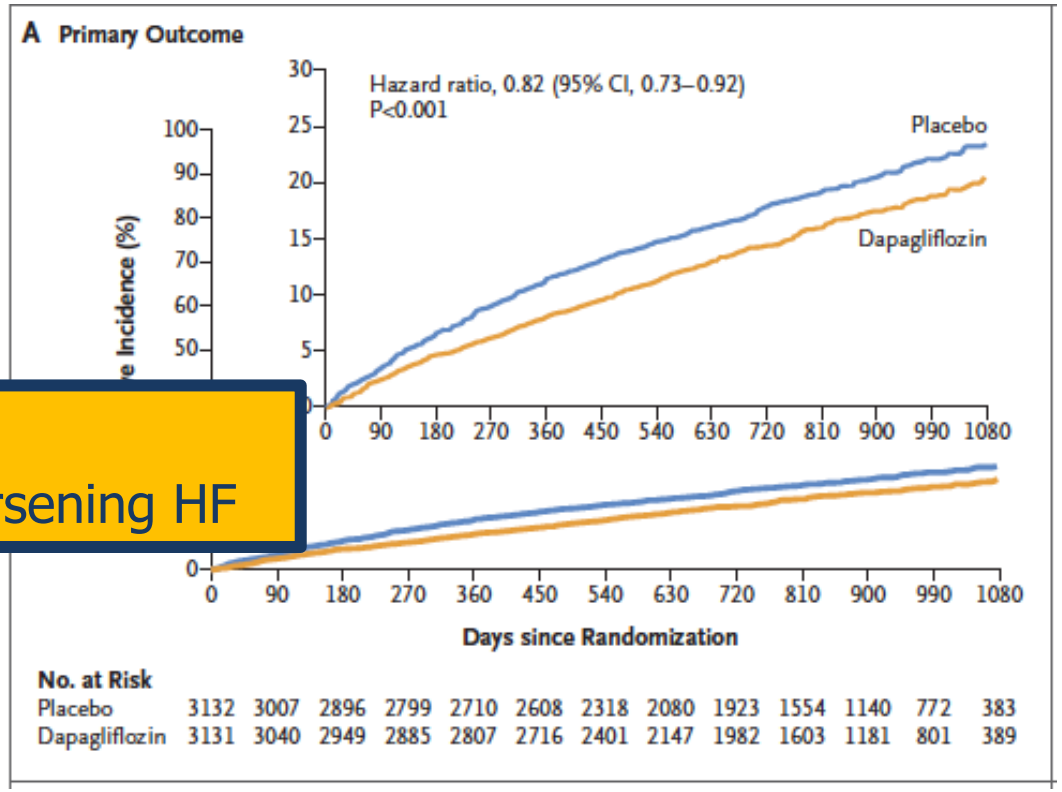


Anker SD. Et al. NJEM 2021

↓ CV death or
↓ hospitalisation for worsening HF

- **N = 5988 patients**
- **EF > 40%**
- **Empagliflozin or placebo**
- **Primary EP:** Composite of CV Death or Hospitalization for Heart Failure

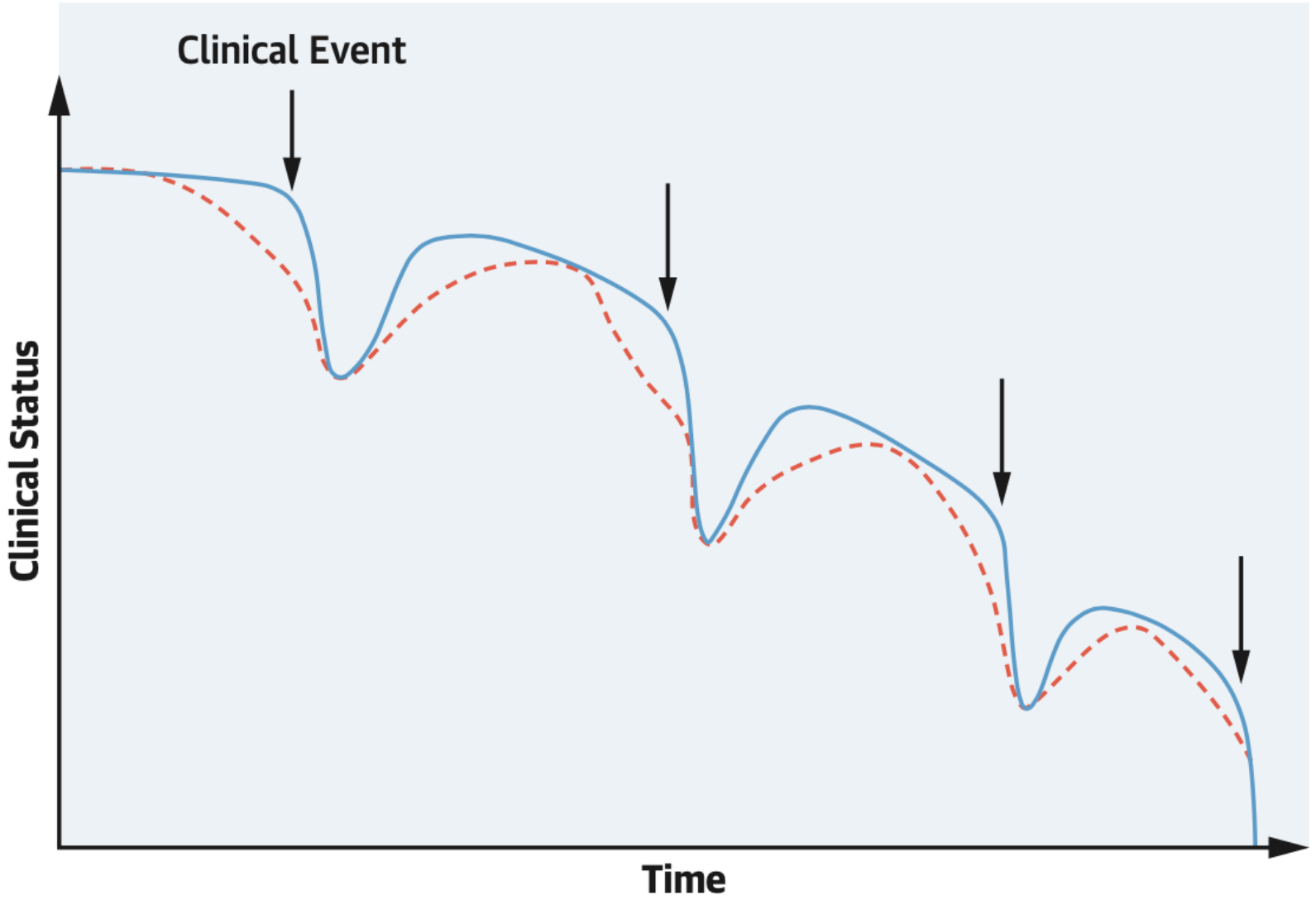
DELIVER trial



Solomon SD. et al. NJEM 2022

- **N = 6263 patients**
- **EF > 40%**
- **Dapagliflozin or placebo**
- **Primary EP:** Composite of **worsening heart failure (unplanned hospitalization or an urgent visit for HF) or cardiovascular death,**

Traditional and New Theories of HF Clinical Course



Greene S et al. JACC 2023

Conclusions

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HFrEF treatment

- Quick introduction
- Quick titration
- No sequential order

HF treatment and titration

- Reduce Mortality
- Reduce morbidity (HF hospitalisation and worsening HF)

Hôpital Erasme

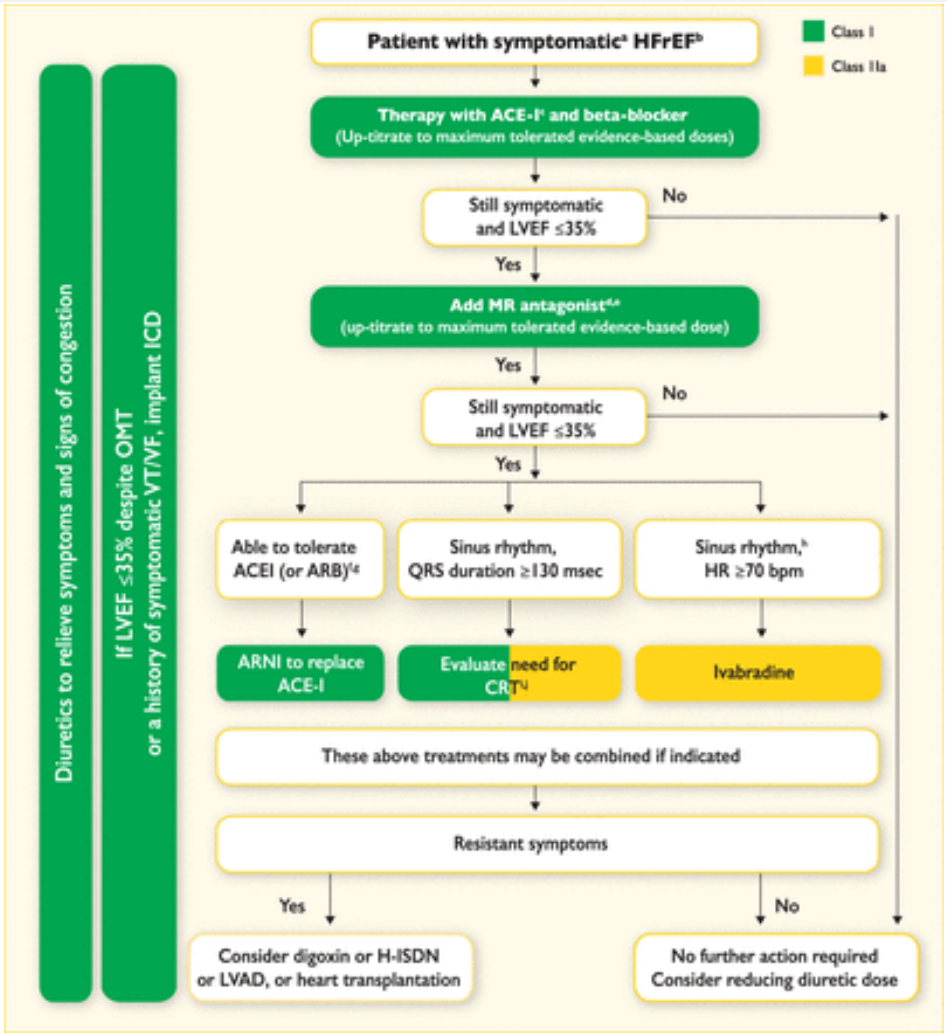
ULB

Merci pour votre attention

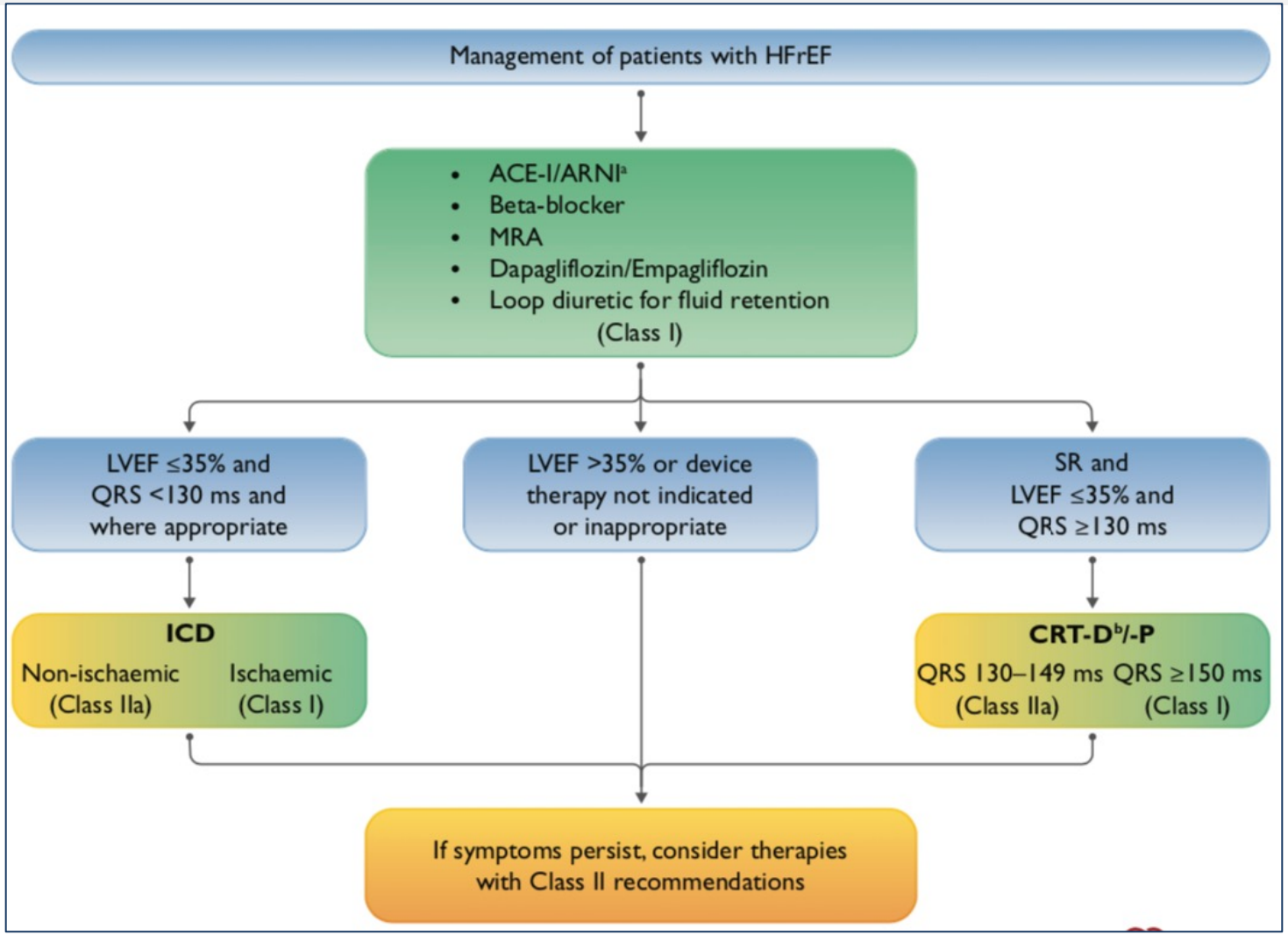
Management of patients with HFrEF

Hôpital Erasme | ULB

2016



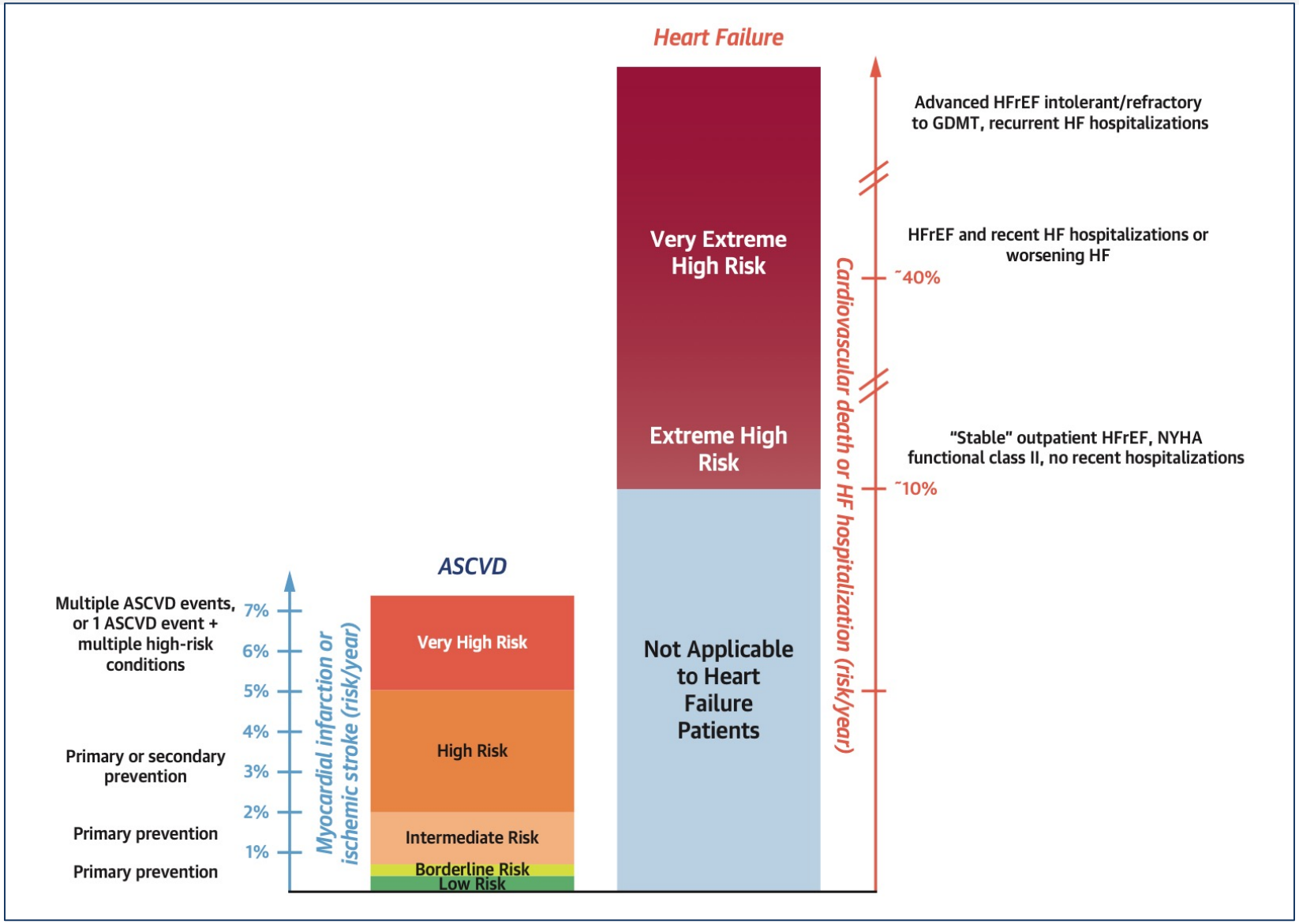
2021



Polikowski P, et al. EHJ 2016
McDonagh T, et al. Eur Heart J 2021

HFrEF patients

Cardiovascular death or HF hospitalization (risk/year)



Greene S et al. JACC 2023

Heart failure - Definition

HF is a clinical syndrome characterized by:

- Cardinal **symptoms** (breathlessness, ankle swelling, fatigue) that may be accompanied by **signs** (elevated jugular venous pressure, pulmonary crackles, peripheral oedema)
- Due to structural and/or functional cardiac abnormality
- Resulting in elevated intracardiac pressures an/or inadequate cardiac output at rest and/or during exercise.
- Demonstration of an underlying cardiac cause is central to the diagnosis of HF.

McDonagh T, et al. Eur Heart J 2021

HF Treatment according to LVEF
HFrEF (≤ 40%)

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CONSENSUS
SOLVD

PARADIGM-HF

MERIT-HF
CIBIS-2
COPERNICUS
SENIOR

RALES
Emphasis HF

DAPA HF
EMPEROR-Reduced

McDonagh T, et al. Eur Heart J 2021