HFA Heart Failure Association
European Society of Cardiology
САНУ СРПСКА АКАДЕМИЈА НАУКА И УМЕТНОСТИ
УНИВЕРЗИТЕТ У БЕОГРАДУ МЕДИЦИНСКИ ФАКУЛТЕТ
KLINIČKI CENTAR SRBIJE
Heart failure Society of Serbia

Prof. dr Petar M. Seferovic, MD, PhD, FESC, FACC

Chair, ESC Task force on Eastern Countries

Co-Editor for Eastern Europe, European Heart Journal

Vice-president, European Society of Cardiology (2020-2022)

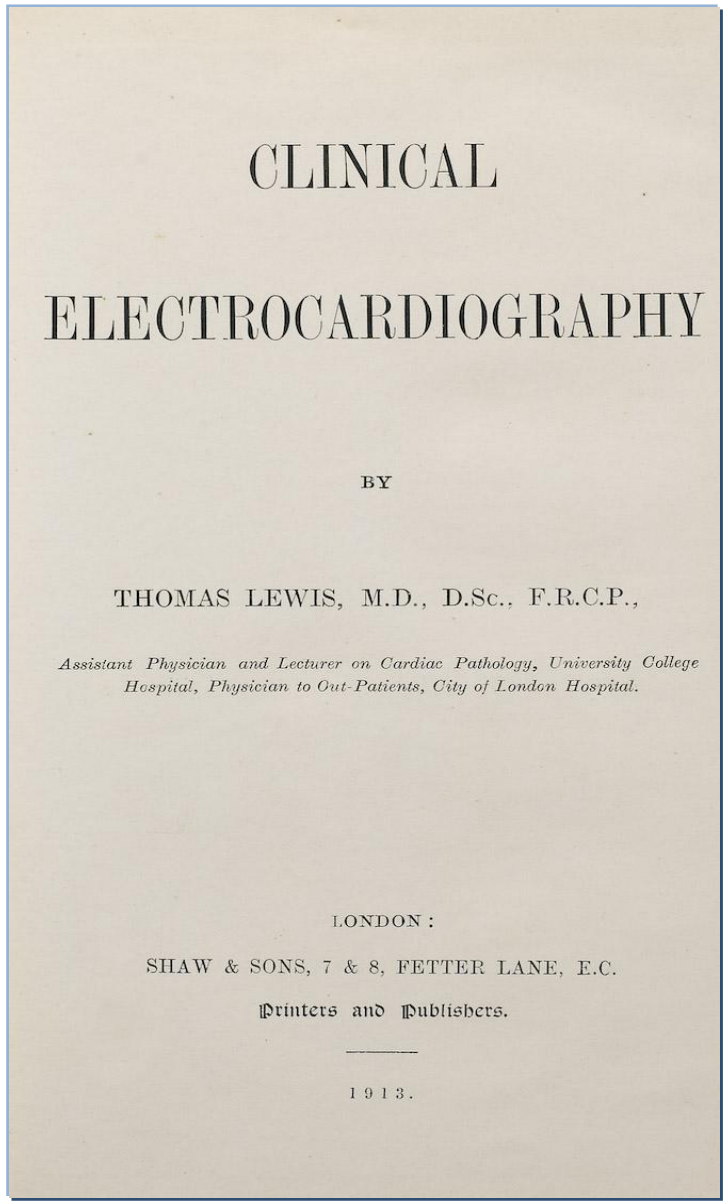
The new insight into conundrum of implementation of four pillars HFrEF treatment

Academician, Serbian Academy of Sciences and Arts

Professor of Cardiology, Belgrade University School of Medicine

President, Heart failure Society of Serbia

Heart failure: The basics of clinical cardiology



CLINICAL

ELECTROCARDIOGRAPHY

BY

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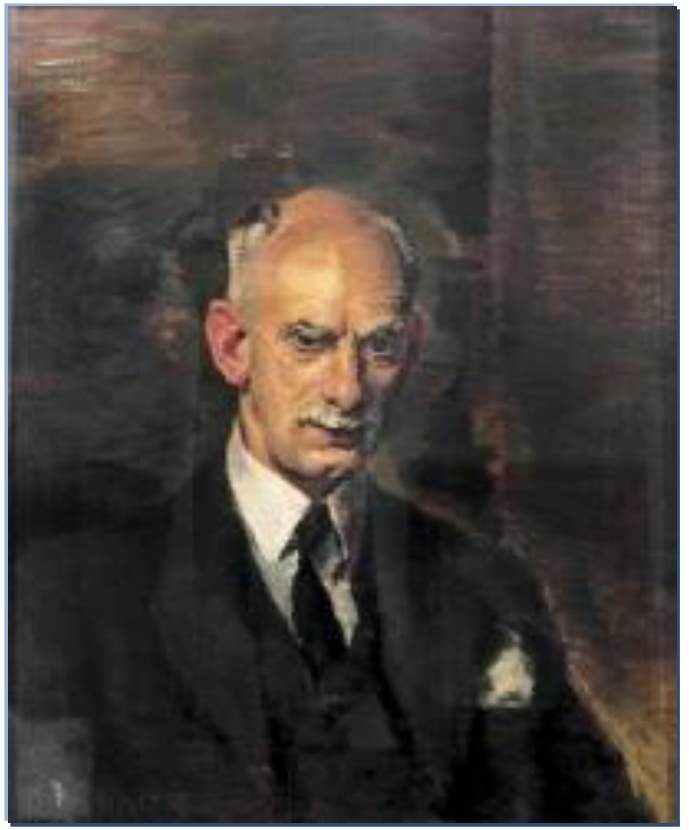
LONDON:

SHAW & SONS, 7 & 8, FETTER LANE, E.C.

Printers and Publishers.

1913.

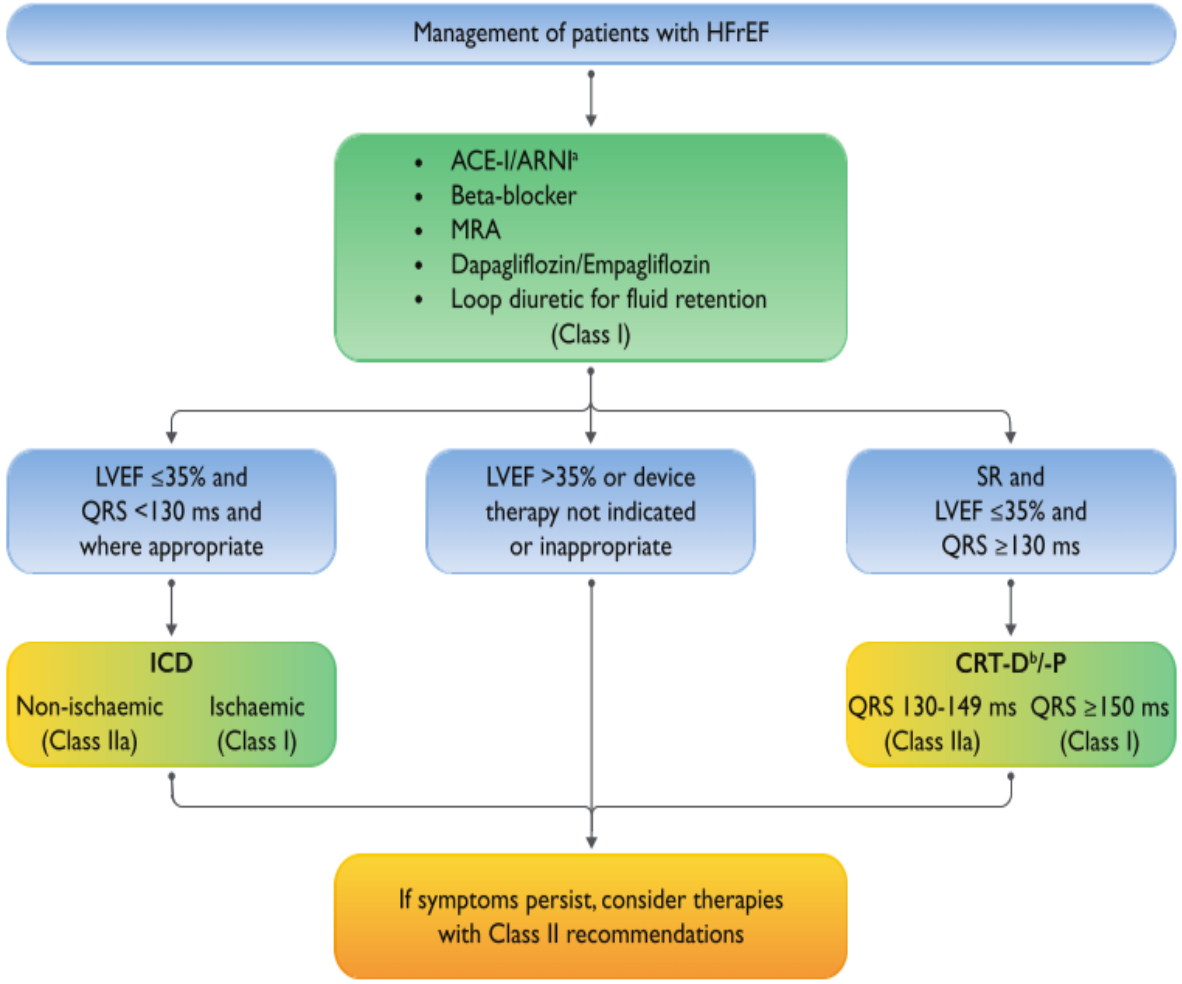


"First and basic task of cardiologist is to know diagnosis and treatment of heart failure"

Sir Thomas Lewis 1913.

ESC
European Society of Cardiology

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



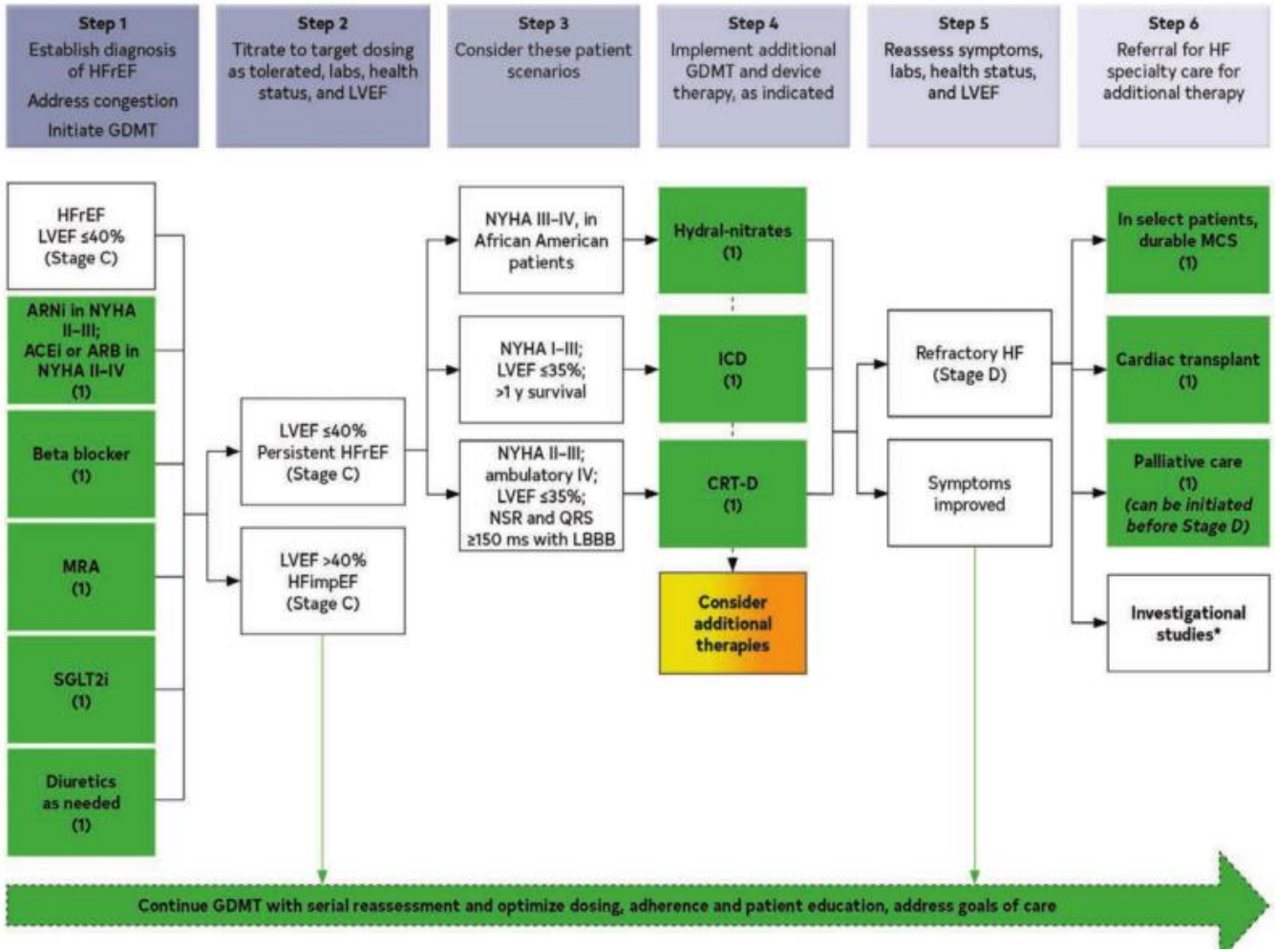
American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY

HFSA
HEART FAILURE SOCIETY OF AMERICA

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure



EHJ 2021;00:1-128; Circulation. 2022;145:00–00

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.3642

POSITION PAPER

How to handle polypharmacy in heart failure. A clinical consensus statement of the Heart Failure Association of the ESC

Davide Stolfo[1,2†], Massimo Iacoviello[3†], Ovidiu Chioncel[4,5], Markus S. Anker[6,7], Antoni Bayes-Genis[8], Frieder Braunschweig[9], Antonio Cannata[10,11], Seif El Hadidi[12], Gerasimos Filippatos[13], Pardeep Jhund[14], Alexandre Mebazaa[15,16], Brenda Moura[17], Massimo Piepoli[18,19], Robin Ray[20], Arsen D. Ristic[21,22], Petar Seferovic[23], Maggie Simpson[24], Hadi Skouri[25], Carlo Gabriele Tocchetti[26], Sophie Van Linthout[27,28], Cristiana Vitale[20], Maurizio Volterrani[29,30], Kalliopi Keramida[31], Sven Wassmann[32], Basil S. Lewis[33], Marco Metra[34], Giuseppe M.C. Rosano[35,36‡], and Gianluigi Savarese[1*‡]

Strategies to improve GDMT implementation in HFrEF

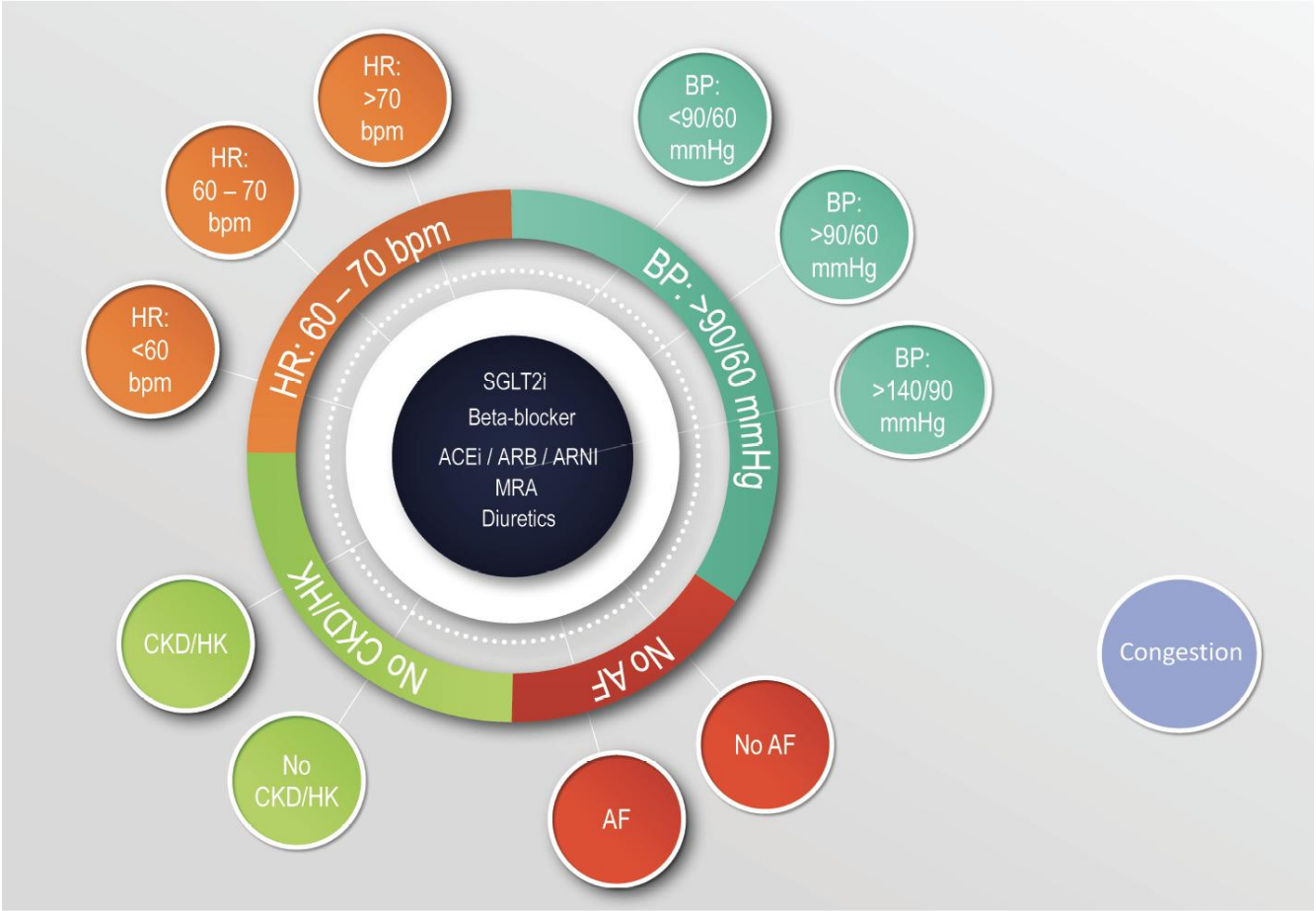
Patient profiling: tailoring medical therapy to specific clinical profile

Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology

Giuseppe M.C. Rosano[1†], Brenda Moura[2,3*†], Marco Metra[4], Michael Böhm[5], Johann Bauersachs[6], Tuvia Ben Gal[7], Stamatis Adamopoulos[8], Magdy Abdelhamid[9], Vasiliki Bistola[10], Jelena Čelutkienė[11], Ovidiu Chioncel[12,13], Dimitrios Farmakis[14], Roberto Ferrari[15,16], Gerasimos Filippatos[17], Loreena Hill[18], Ewa A. Jankowska[19], Tiny Jaarsma[20,21], Pardeep Jhund[22], Mitja Lainscak[23,24], Yuri Lopatin[25], Lars H. Lund[26], Davor Milicic[27], Wilfried Mullens[28,29], Fausto Pinto[30], Piotr Ponikowski[31], Gianluigi Savarese[26], Thomas Thum[32], Maurizio Volterrani[1], Stefan D. Anker[33], Petar M. Seferovic[34,35], and Andrew J.S. Coats[36]

Recommendations for 9 clinical profiles:

1. **Low BP and high HR,**
2. **Low BP and low HR,**
3. **Normal BP and low HR,**
4. **Normal BP and high HR,**
5. **AF + normal BP,**
6. **AF + low BP,**
7. **Chronic kidney disease**
8. **Predischarge**
9. **Hypertension despite GDMT**



Rosano G et al. European Journal of Heart Failure (2021) 23, 872–881

HEART FAILURE AND CARDIOMYOPATHIES

EDITOR'S CHOICE

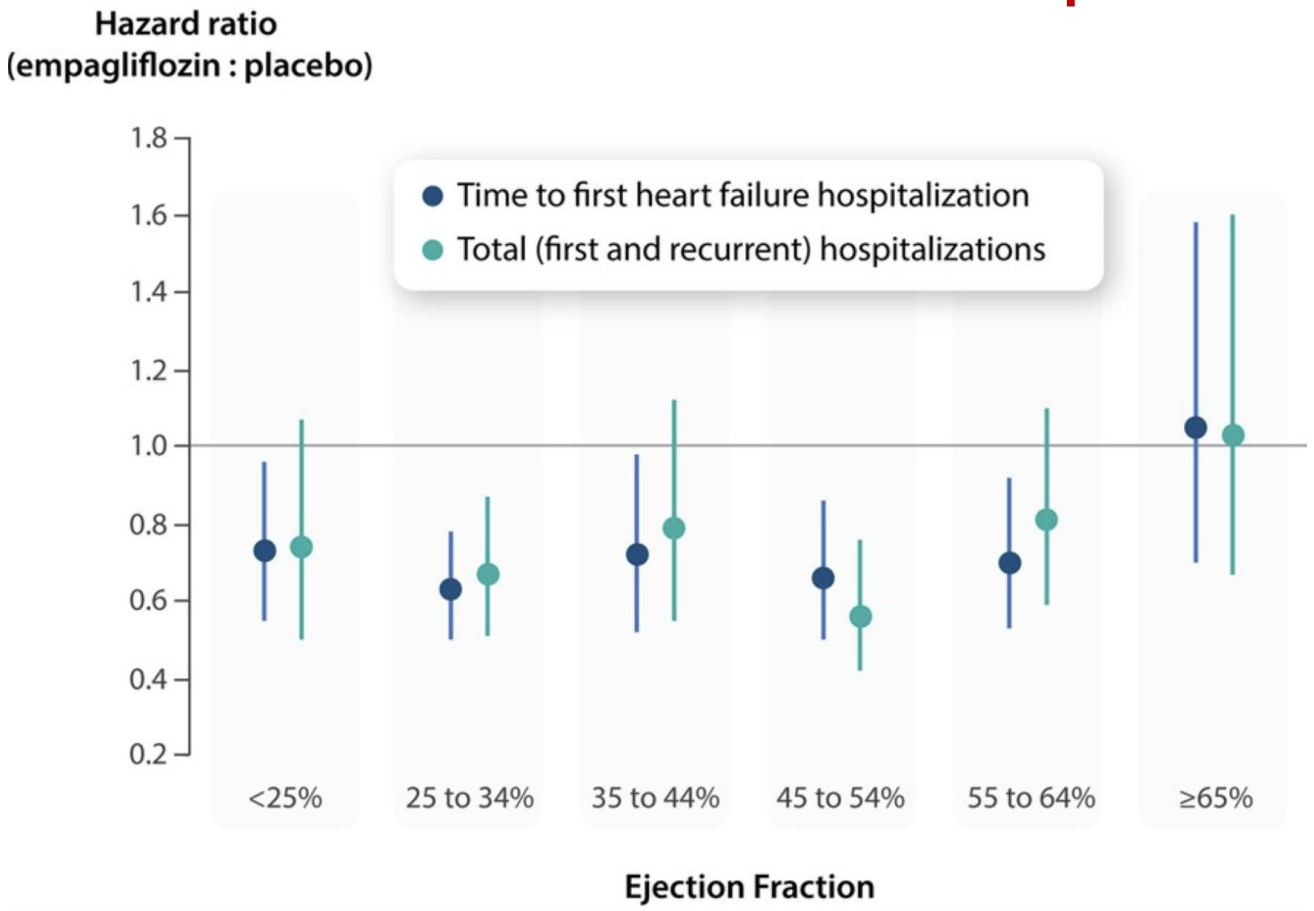
Effect of empagliflozin in patients with heart failure across the spectrum of left ventricular ejection fraction

Javed Butler and others

European Heart Journal, Volume 43, Issue 5, 1 February 2022, Pages 416–424,

Article highlight:

EMPEROR-pooled analysis: the magnitude of the effect of empagliflozin on HF outcomes and health status was similar across LVEF <25% to <65%, but it was attenuated in patients with LVEF ≥65%.



JOURNAL ARTICLE EDITOR'S CHOICE

Great Debate: SGLT2 inhibitors should be first-line treatment in heart failure with reduced ejection fraction FREE

Milton Packer, John G F Cleland, Johann Bauersachs ✉ Author Notes

EHJ
Great debate

- **With an introduction by J Bauersachs, M. Packer and J. Cleland discuss scientific evidence for the use of SGLT2 inhibitors as first-line HFrEF treatment.**

SGLT2 inhibitors should be first line treatment in heart failure with reduced ejection fraction

Pro	Contra
DAPA-HF and EMPEROR-Reduced demonstrate early and sustained reduction of CV death/HF hospitalizations	Only patients failing on GRMT were enrolled in DAPA-HF and EMPEROR-Reduced
SGLT2i are among the four foundational drugs for HFrEF and can add to the efficacy of the other three	Inconsistent effect of SGLT2i on mortality; most HF hospitalizations not prevented
When all foundational drugs are started within one week, the ordering does not matter	DAPA-MI failed to show SGLT2i reduced HF or all-cause hospitalizations or deaths
SGLT2i do not require dose adjustment or uptitration; the starting dose of these drugs is the target dose	All-cause hospitalizations are more important drivers of healthcare costs, HF causes <30% of all admissions
Modeling analyses suggest greatest benefit when SGLT2i are initiated first	Effect of SGLT2i on morbidity/mortality modest versus β-blocker, MRA or ARNI
SGLT2i can facilitate the safety and tolerability of other foundational drugs for HF	Many patients in trials had few symptoms and little symptom benefit from SGLT2i
	Adjusting diuretics may have a similar effect as SGLT2i on symptoms/congestion

European Heart Journal, Volume 45, Issue 25, 1 July 2024, Pages 2186–2196

Simultaneous HF drug uptitration decreases mortality/HF hospitalization: A multinational observational study (US, UK and Sweden)

Look-back period | **Index:** 2016–2019 | **Analysis period:** 1-year results

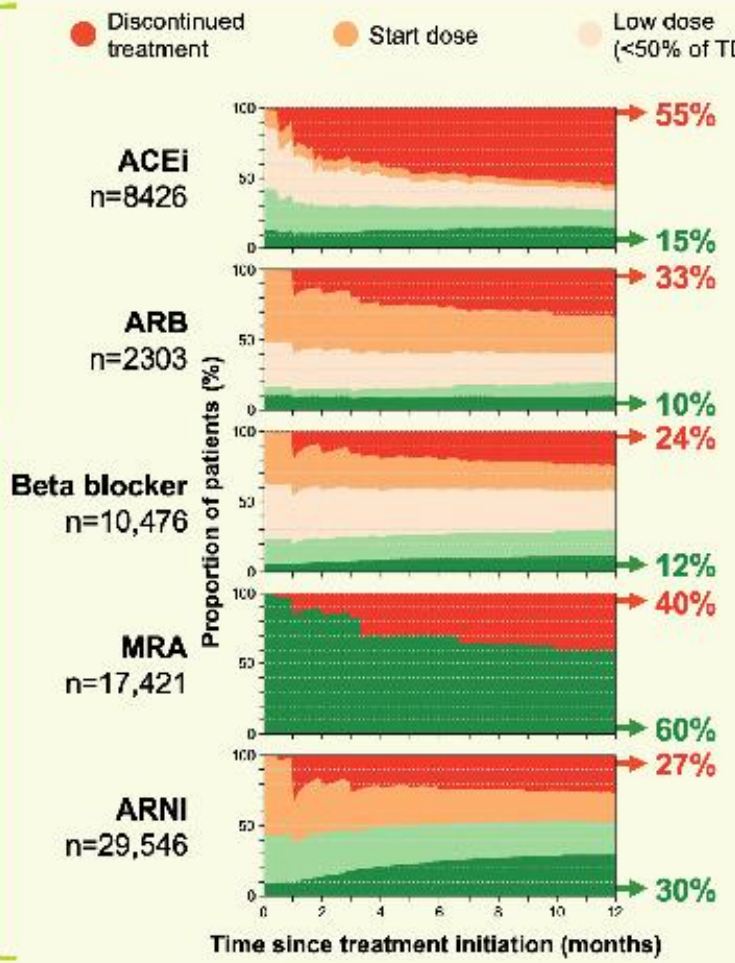
Patients
68,172 new users

Drug-naïve patients → HHF discharge → New use of GDMT

Aim

How are GDMTs initiated and used?

What are the risks of HHF and death after GDMT initiation?



Risks of HHF or death (events/100 patient-years)

	HHF or ACD*	HHF	ACD*
ACEi	40.0	18.9	24.0
ARB	43.3	24.4	21.1
Beta blocker	45.9	22.4	28.8
MRA	53.6	27.9	31.0
ARNI	86.9	46.8	21.3

Treatment initiation immediately after HHF. *Sweden and UK only.

The high risks do not relate to the effectiveness of the drugs, but the point in the HF disease journey at which the drug has been initiated.

Conclusion

New initiation of GDMT was followed by consistent patterns of low up-titration and early discontinuation in the three countries involved.

During GDMT utilisation, patients are at high risk, demonstrating the urgent need to move away from a prolonged, sequential approach.

ACD, all-cause death; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; GDMT, guideline-directed medical therapy; HF, heart failure; HHF, hospitalisation for heart failure; MRA, mineralocorticoid receptor antagonist; TD, target dose.

Eur J Heart Fail . 2021 Jun 15. doi: 10.1002/ejhf.2271

EDITOR'S CHOICE

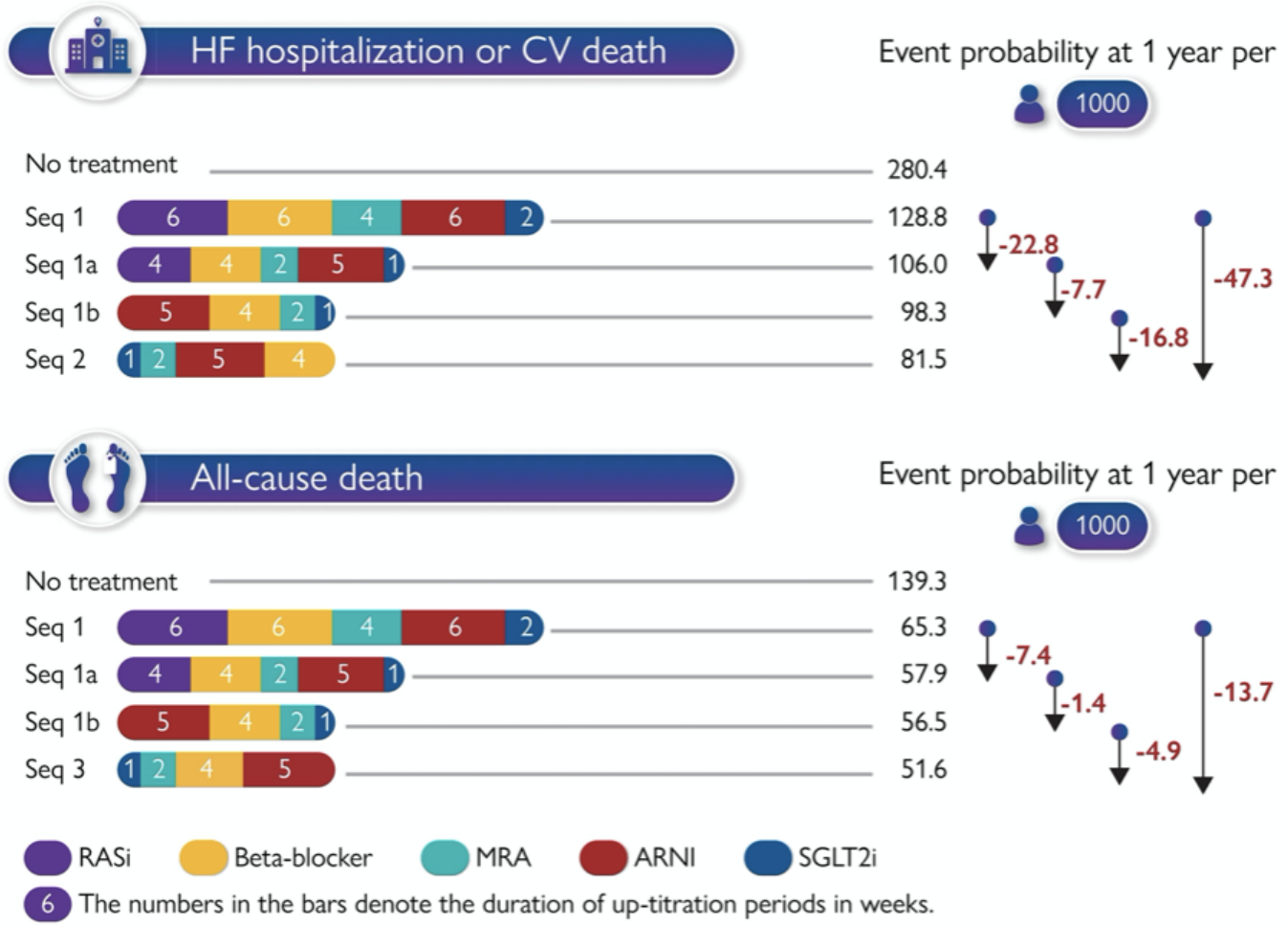
Accelerated and personalized therapy for heart failure with reduced ejection fraction FREE

Li Shen and others

European Heart Journal, Volume 43, Issue 27, 14 July 2022, Pages 2573–2587,

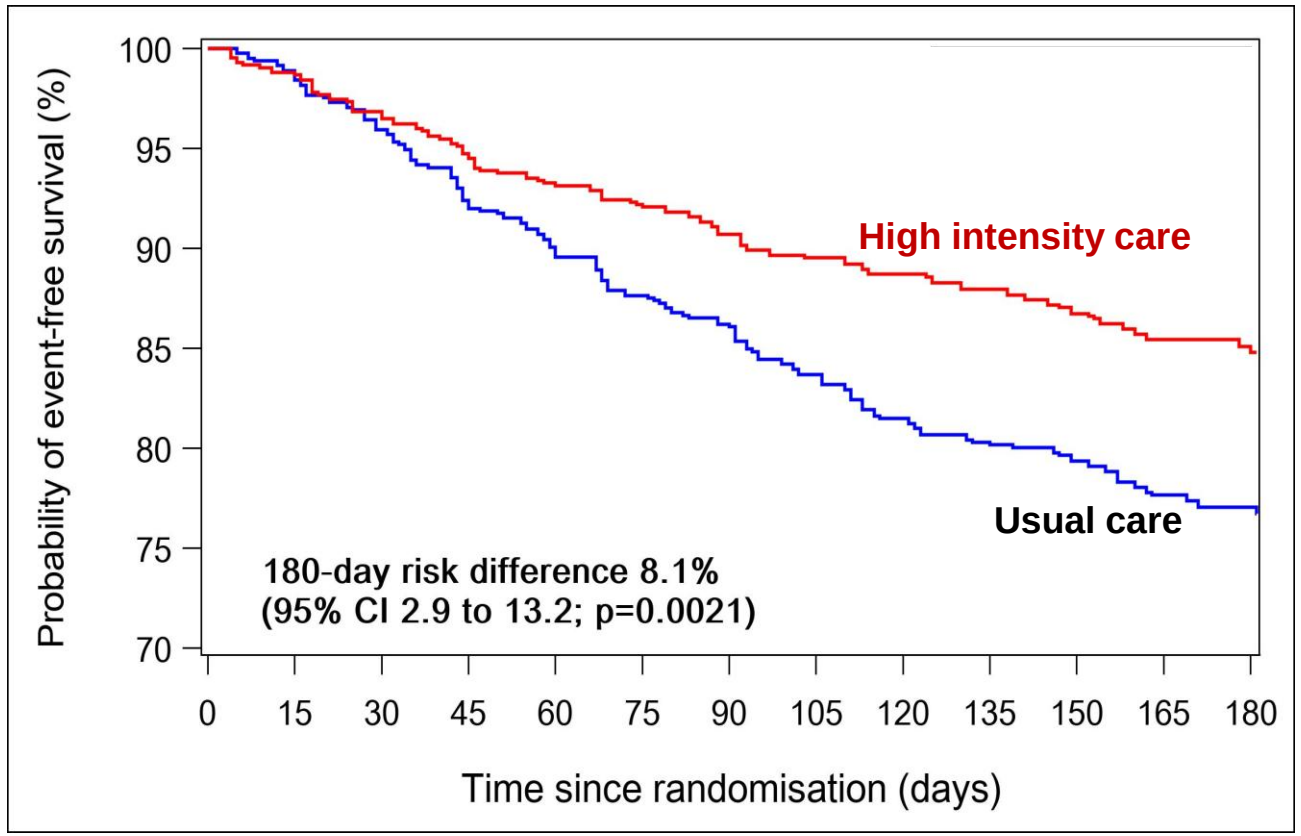
Article highlight:

Accelerated up-titration and optimized ordering can prevent at least 14 deaths and 47 HF hospitalisations/CV deaths per 1000 treated HFrEF patients over the first 12 months.

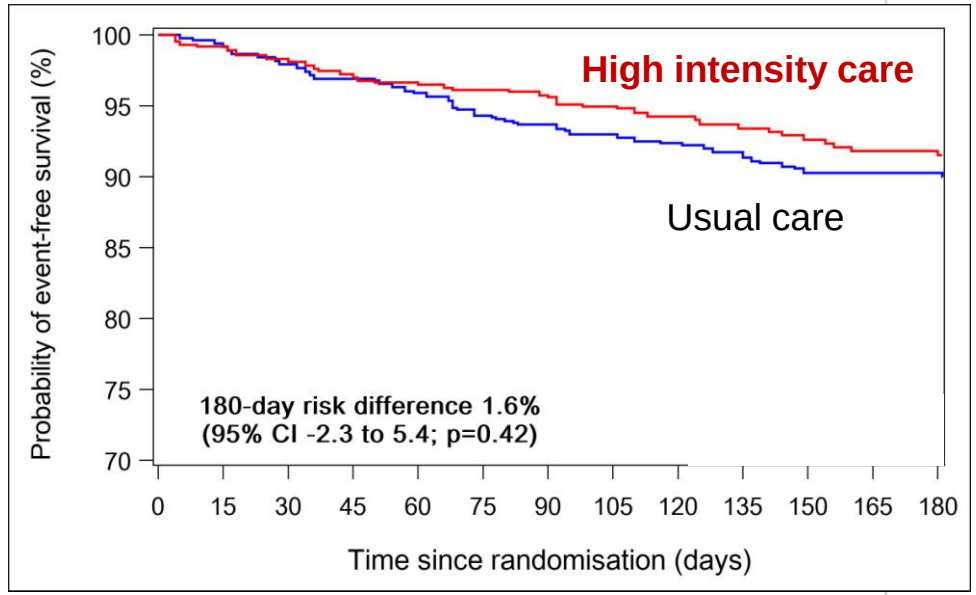


STRONG-HF: Primary Endpoint

Primary endpoint:
180-Day Readmission for HF or All-Cause Death



180-Day All-Cause Death



Mebazaa A et al. The Lancet 2022

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

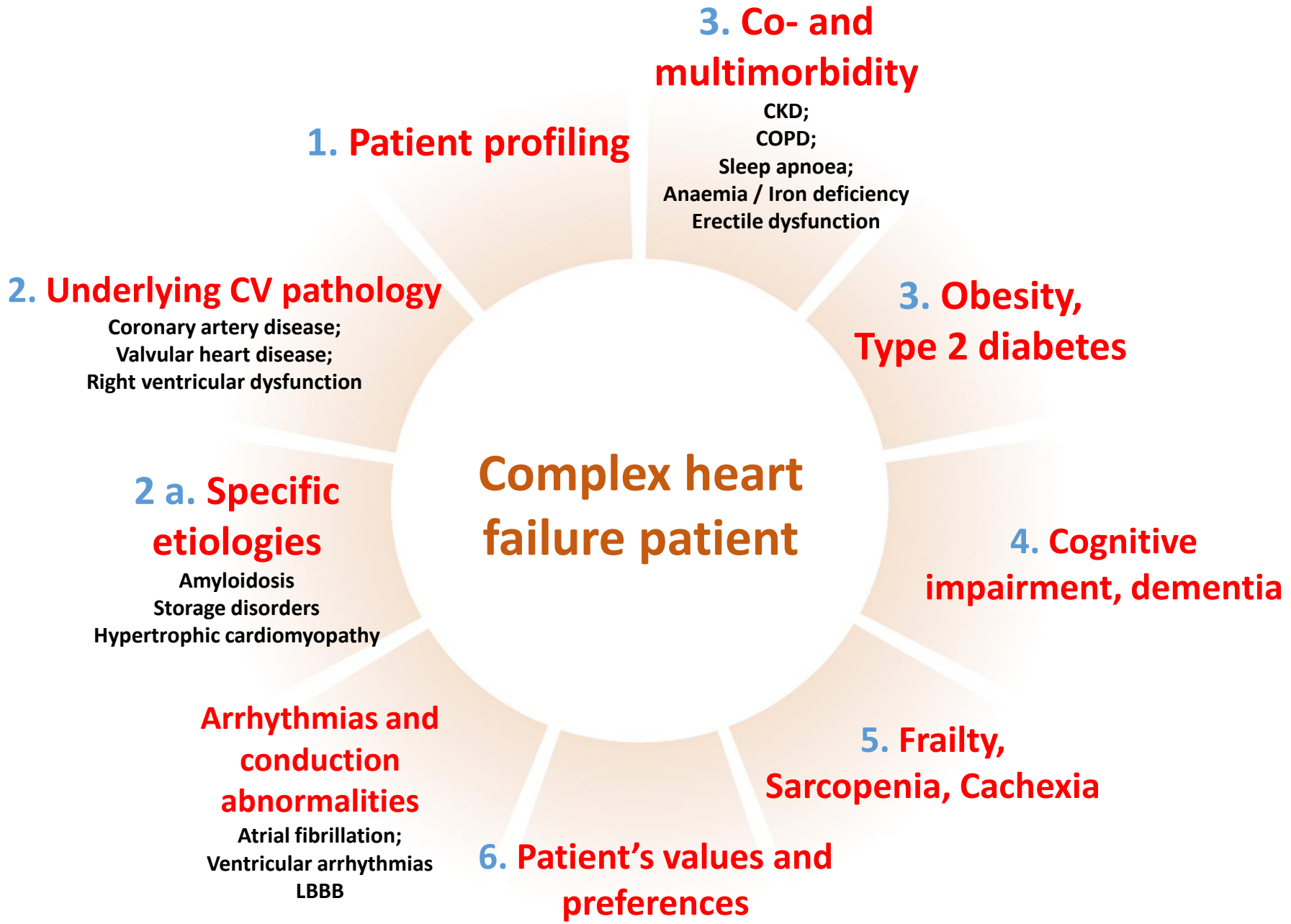
Recommendation	Class[a]	Level[b]
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.[c,d,e]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

This recommendation is based on the results of the STRONG-HF trial.
Evidence-based GDMT in the STRONG-HF included: ACEI/ARB/ARNI, BB i MRA.

ESC Guidelines recommend addition of dapagliflozin or empagliflozin to neurohumoral inhibitors, based on recent evidence.

Mc Donagh T et al. European Heart Journal (2023) 00, 1–13

Complexity of heart failure and treatment effect



ESC European Society of Cardiology

European Journal of Heart Failure (2023) **25**, 776–791
doi:10.1002/ejhf.2874

CONSENSUS STATEMENT

Worsening of chronic heart failure: definition, epidemiology, management and prevention. A clinical consensus statement by the Heart Failure Association of the European Society of Cardiology

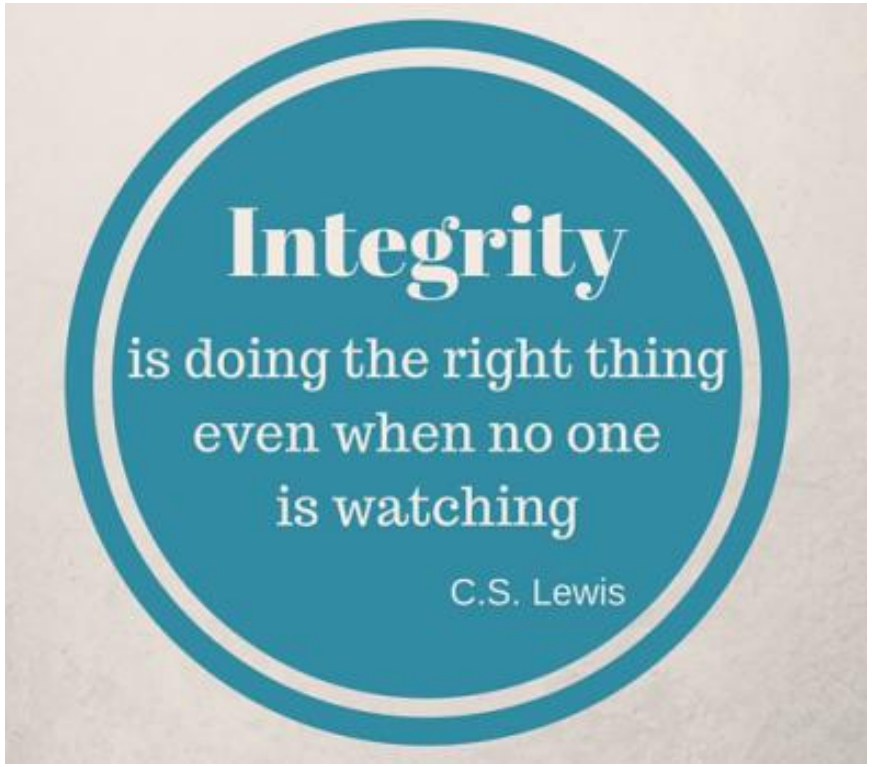
Marco Metra[1#], Daniela Tomasoni[1#], Marianna Adamo[1*], Antoni Bayes-Genis[2], Gerasimos Filippatos[3], Magdy Abdelhamid[4], Stamatis Adamopoulos[5], Stefan D. Anker[6], Laura Antohi[7,8], Michael Böhm[9], Frieder Braunschweig[10], Tuvia Ben Gal[11], Javed Butler[12], John G.F. Cleland[13], Alain Cohen-Solal[14], Kevin Damman[15], Finn Gustafsson[16], Loreena Hill[17], Ewa A. Jankowska[18], Mitja Lainscak[19], Lars H. Lund[10], Theresa McDonagh[20], Alexandre Mebazaa[21], Brenda Moura[22,23], Wilfried Mullens[24], Massimo Piepoli[25,26], Piotr Ponikowski[18], Amina Rakisheva[27], Arsen Ristic[28], Gianluigi Savarese[10], Petar Seferovic[28], Rajan Sharma[29], Carlo Gabriele Tocchetti[30], Mehmet Birhan Yilmaz[31], Cristiana Vitale[32], Maurizio Volterrani[32], Stephan von Haehling[33,34], Ovidiu Chioncel[7,8], Andrew J.S. Coats[35], and Giuseppe Rosano[32]

The art of treating heart failure

HFA Heart Failure Association
European Society of Cardiology

Clinical integrity in overcoming the hurdles

in four pillars treatment

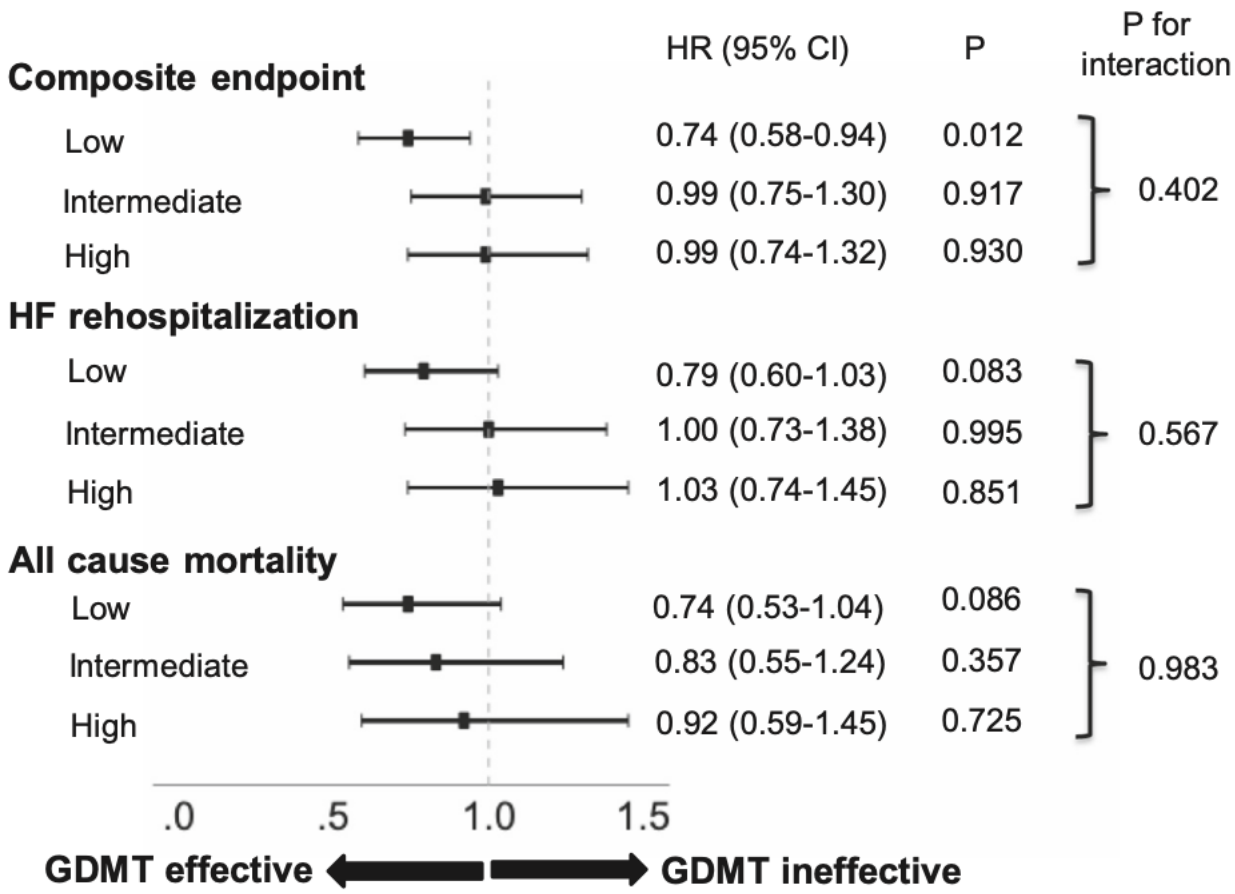


- Hypotension
- Electolyte disbalance
- Worsening renal function

Low blood pressure and guideline-directed medical therapy in patients with heart failure with reduced ejection fraction

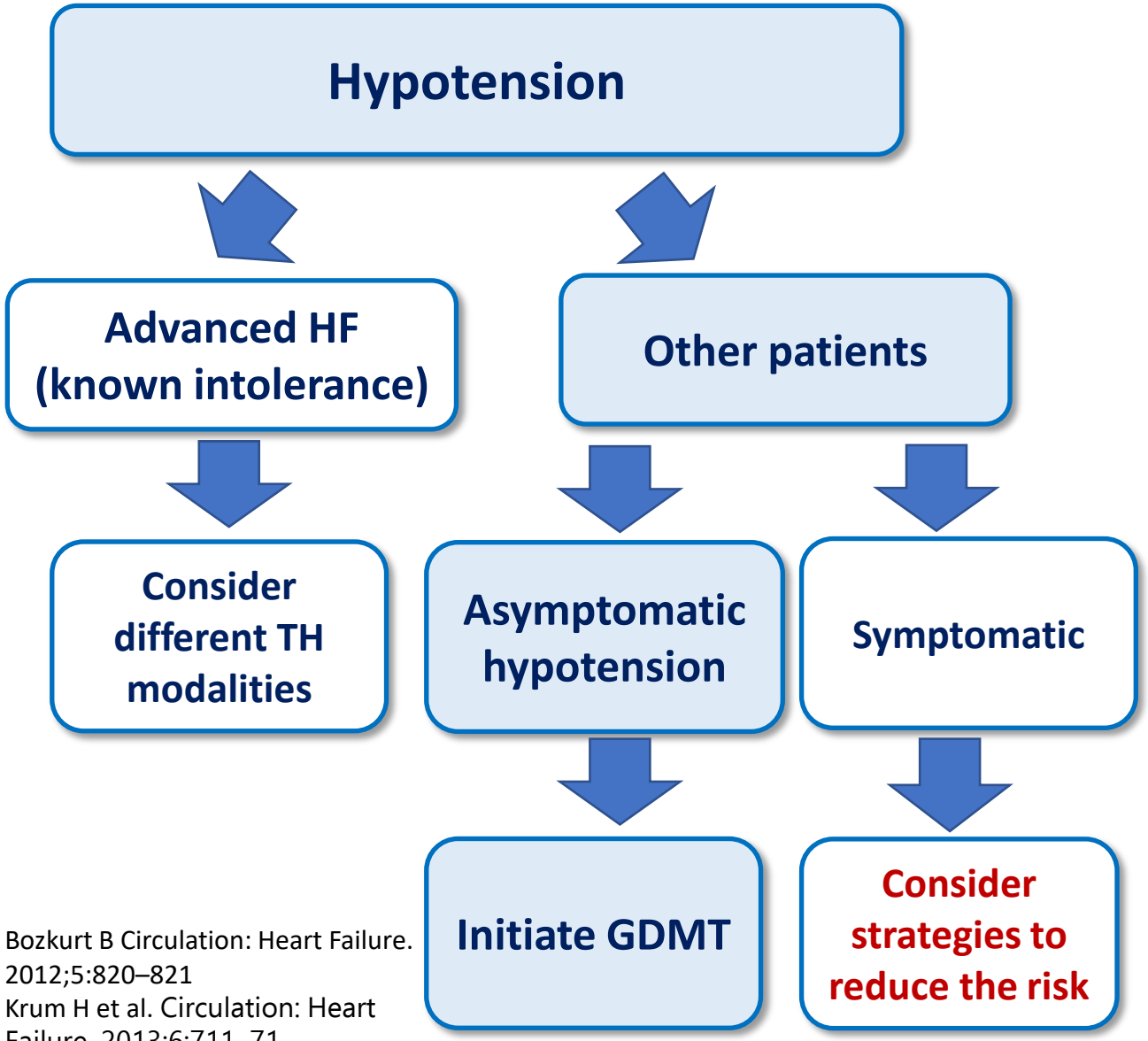
Patients with hypotension derive benefits from GDMT: real-world data

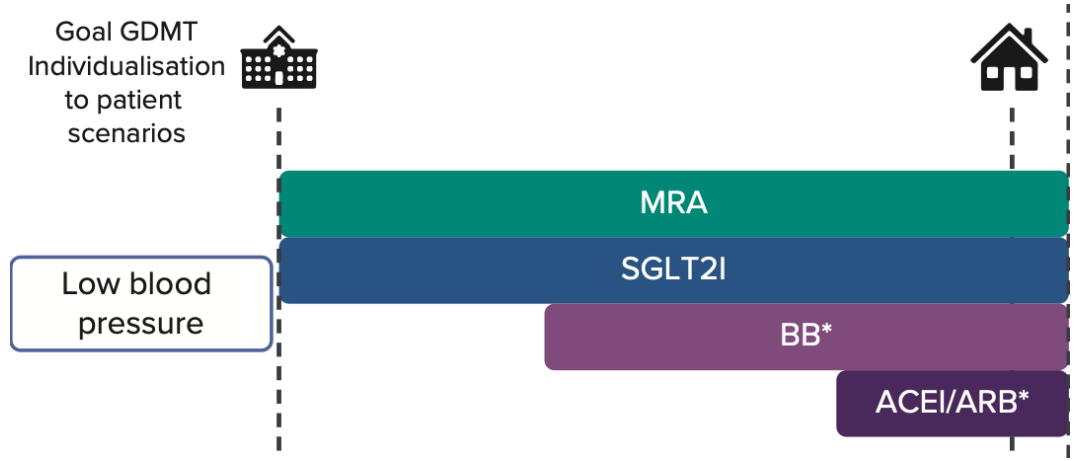
- 2043 consecutive patients with HF and left ventricular ejection fraction (LVEF) < 50% in the WET-HF registry in Japan.
- 708 (34.7%) patients had lower discharge BP (≤ 100 mmHg),
- Among patients with lower BP, GDMT prescription rate was 62.7%, and GDMT use was associated with decreased adverse events (HR:0.74, 95%CI:0.58–0.94).



Izumi K et al. International Journal of Cardiology 370 (2023) 255–262

Tackling hypotension in GDMT implementation





Strategies to reduce the risk:

- SGLT2i and MRA: neutral effect on BP.
- BB: modest effect
- Appropriate decongestion.
- Avoid of unnecessary drugs with hypotensive effect.
- Start low and go slow targeting maximum tolerated dose.

Bozkurt B Circulation: Heart Failure. 2012;5:820–821
Krum H et al. Circulation: Heart Failure. 2013;6:711–71

ESC European Society of Cardiology

European Journal of Heart Failure (2025) **27**, 707–722
doi:10.1002/ejhf.3618

POSITION PAPER

Clinical management and therapeutic optimization of patients with heart failure with reduced ejection fraction and low blood pressure. A clinical consensus statement of the Heart Failure Association (HFA) of the ESC

Hadi Skouri[1,2*†], Nicolas Girerd[3†], Luca Monzo[3], Mark C. Petrie[4], Michael Böhm[5], Marianna Adamo[6], Wilfried Mullens[7,8], Gianluigi Savarese[9], Mehmet Birhan Yilmaz[10], Offer Amir[11], Antoni Bayes-Genis[12], Biykem Bozkurt[13], Javed Butler[14,15], Ovidiu Chioncel[16], Alexandre Mebazaa[17], Jose L. Merino[18], Brenda Moura[19], Piotr Ponikowski[20], Petar Seferovic[21], Giuseppe M.C. Rosano[22,23,24,25], and Marco Metra[6]

Electrolyte disorders

Hyperkalaemia	▪ MRA contraindicated if K+ >5,5 mmol/L. ▪ Higher risk: elderly, DM, CKD, Concomitant use of ACEi/ARB	▪ **Switch from ACEi-ARB to ARNI** ▪ **Reduce the dose of MRA, and RAASi** ▪ **Use SGLT2i**
Hyponatraemia	▪ MRA contraindicated if Na+ <125 mmol/L. ▪ Higher risk: loop diuretics and/or thiazides.	▪ **Reduce diuretic dose** ▪ **Stop thiazide.**

SGLT2 inhibitors have a neutral effect on serum electrolytes.

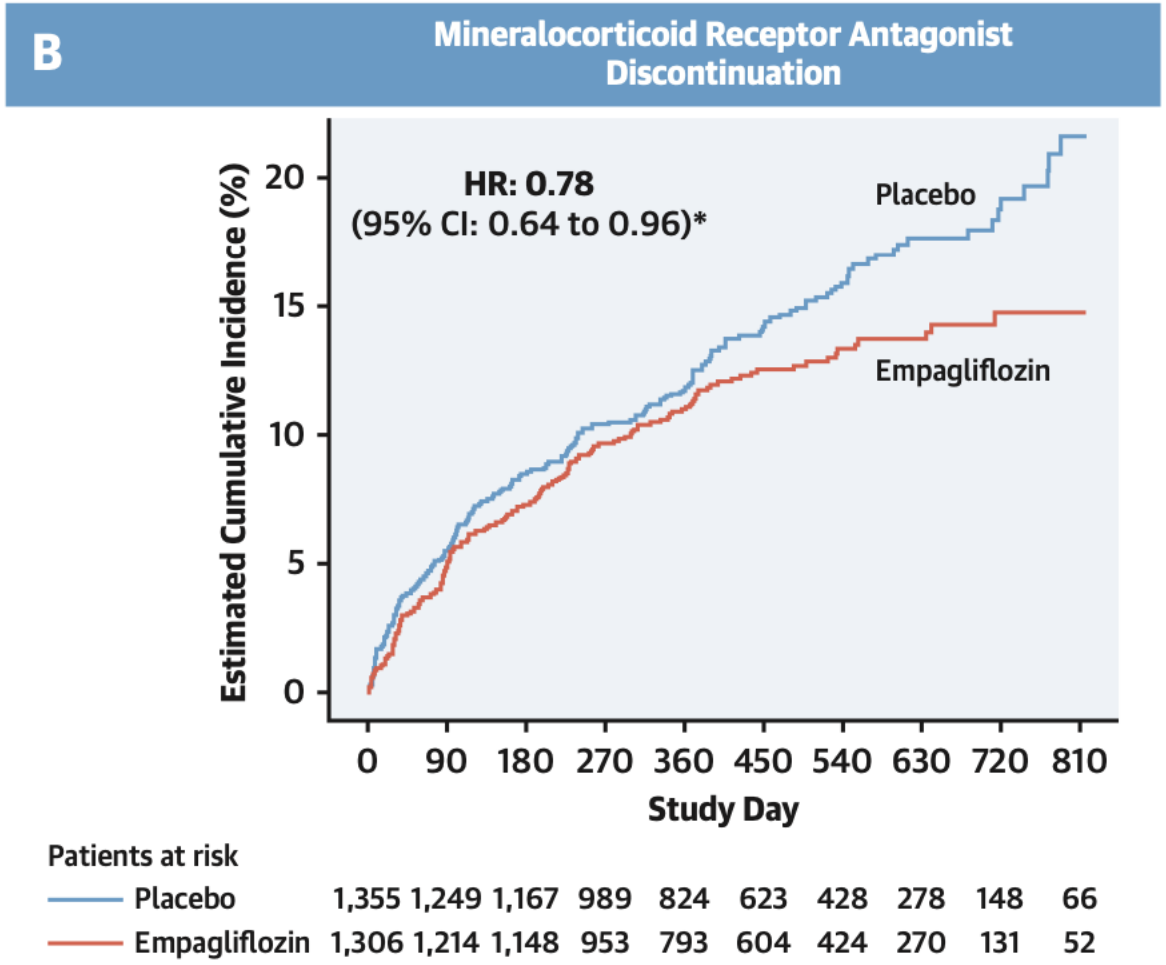
Cautela J et al. European Journal of Heart Failure (2020) 22, 1357–1365

Interplay of Mineralocorticoid Receptor Antagonists and Empagliflozin in Heart Failure

EMPEROR-Reduced

Empagliflozin can facilitate the use of MRA

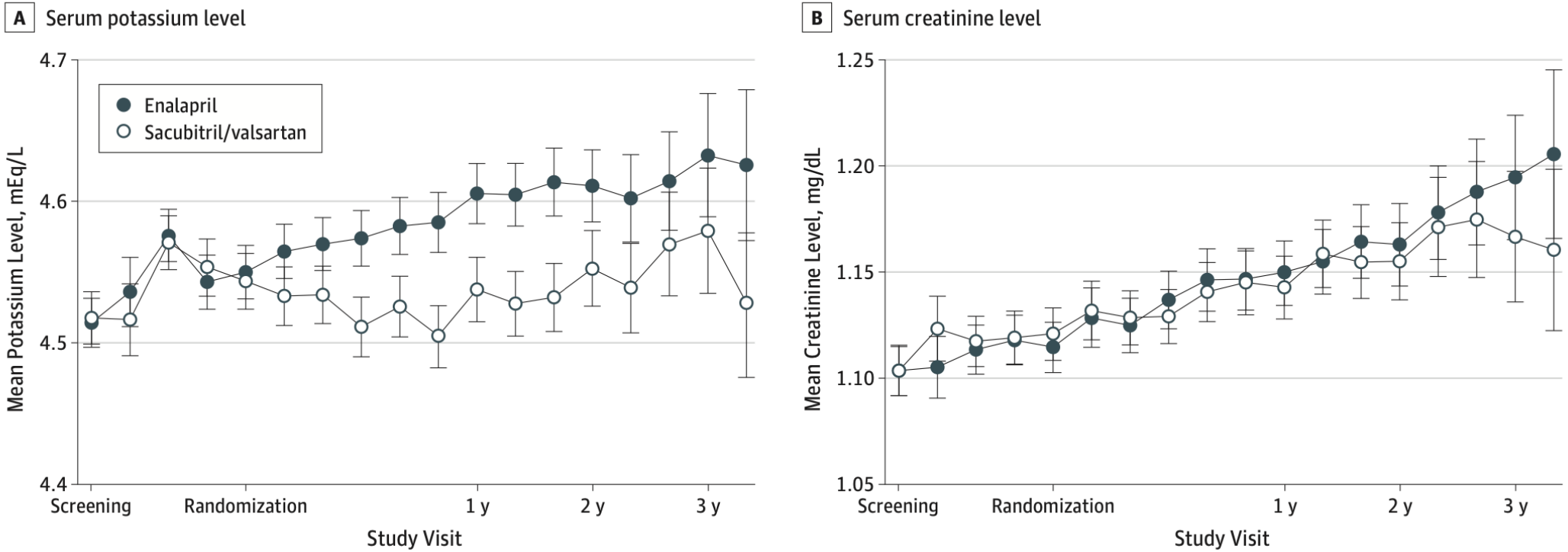
- Secondary analysis that compared the effects of empagliflozin vs placebo in 3,730 HFrEF patients, of whom 71% used MRAs at randomization.
- The use of MRAs did not influence the effect of empagliflozin to reduce adverse HF and renal outcomes.
- Treatment with empagliflozin was associated with less discontinuation of MRAs.



Ferreira, J.P. et al. J Am Coll Cardiol. 2021;77(11):1397-407.

ARNI can reduce the risk of hyperkalemia

Reduced Risk of Hyperkalemia During Treatment of Heart Failure With Mineralocorticoid Receptor Antagonists by Use of Sacubitril/Valsartan Compared With Enalapril
A Secondary Analysis of the PARADIGM-HF Trial



- **Severe hyperkalemia was less likely with ARNI compared to enalapril, without any difference in renal function.**
- **ARNI could reduce the risk of hyperkalemia when MRAs are combined with other RAS inhibitors.**

Desai A et al. JAMA Cardiol. 2017;2(1):79-85.

Hyperkalemia and potassium binders

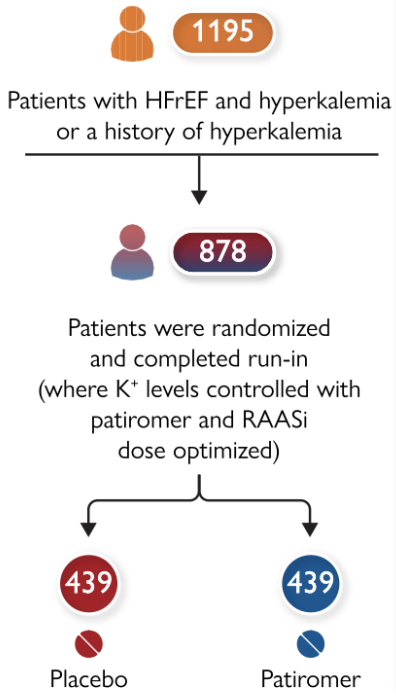
Patiromer for the management of hyperkalemia in heart failure with reduced ejection fraction: the DIAMOND trial

Javed Butler[1,2*†], Stefan D. Anker[3,4,5,6*†], Lars H. Lund[7,8], Andrew J.S. Coats[9], Gerasimos Filippatos[10,11], Tariq Jamal Siddiqi[1,2], Tim Friede[12,13,14], Vincent Fabien[15], Mikhail Kosiborod[16,17], Marco Metra[18], Ileana L. Piña[19], Fausto Pinto[20], Patrick Rossignol[21,22], Peter van der Meer[23], Cecilia Bahit[24], Jan Belohlavek[25], Michael Böhm[26], Jasper J. Brugts[27], John G.F. Cleland[28], Justin Ezekowitz[29], Antoni Bayes-Genis[30], Israel Gotsman[31], Assen Goudev[32], Irakli Khintibidze[33], Joann Lindenfeld[34], Robert J. Mentz[35], Bela Merkely[36], Eliodoro Castro Montes[37], Wilfried Mullens[38], Jose C. Nicolau[39,40], Aleksandr Parkhomenko[41], Piotr Ponikowski[42], Petar M. Seferovic[43,44], Michele Senni[45], Evgeny Shlyakhto[46], Alain Cohen-Solal[47], Peter Szecsödy[15], Klaus Jensen[15], Fabio Dorigotti[15], Matthew R. Weir[48], and Bertram Pitt[49]

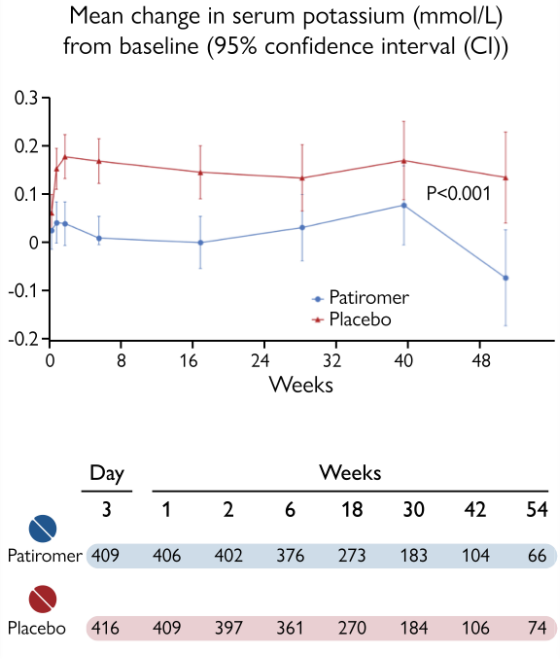
- A total of 1195 patients with HFrEF and current or a history of RAASi-related hyperkalemia were enrolled.
- Goal optimization of the RAASi therapy ≥50% target dose of ACEI/ARB/ARNI, and 50 mg of MRA.
- The use of patiromer reduced the risk of:
  - ✓Hyperkalemia
  - ✓MRA discontinuation or dose reduction.
- The win-ratio for RASi use and hyper-K related morbidity events was favoured by patiromer use.

Patiromer use in patients with heart failure and reduced ejection fraction (HFrEF) with hyperkalemia (HK)

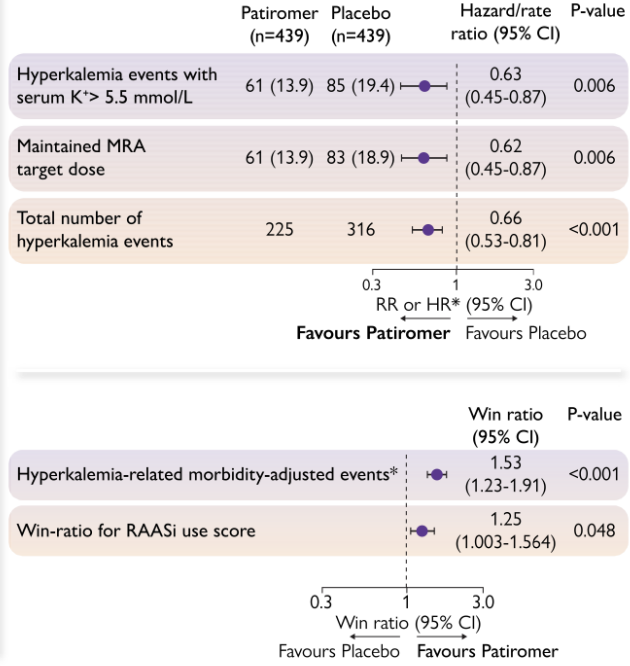
Study design



Primary endpoint



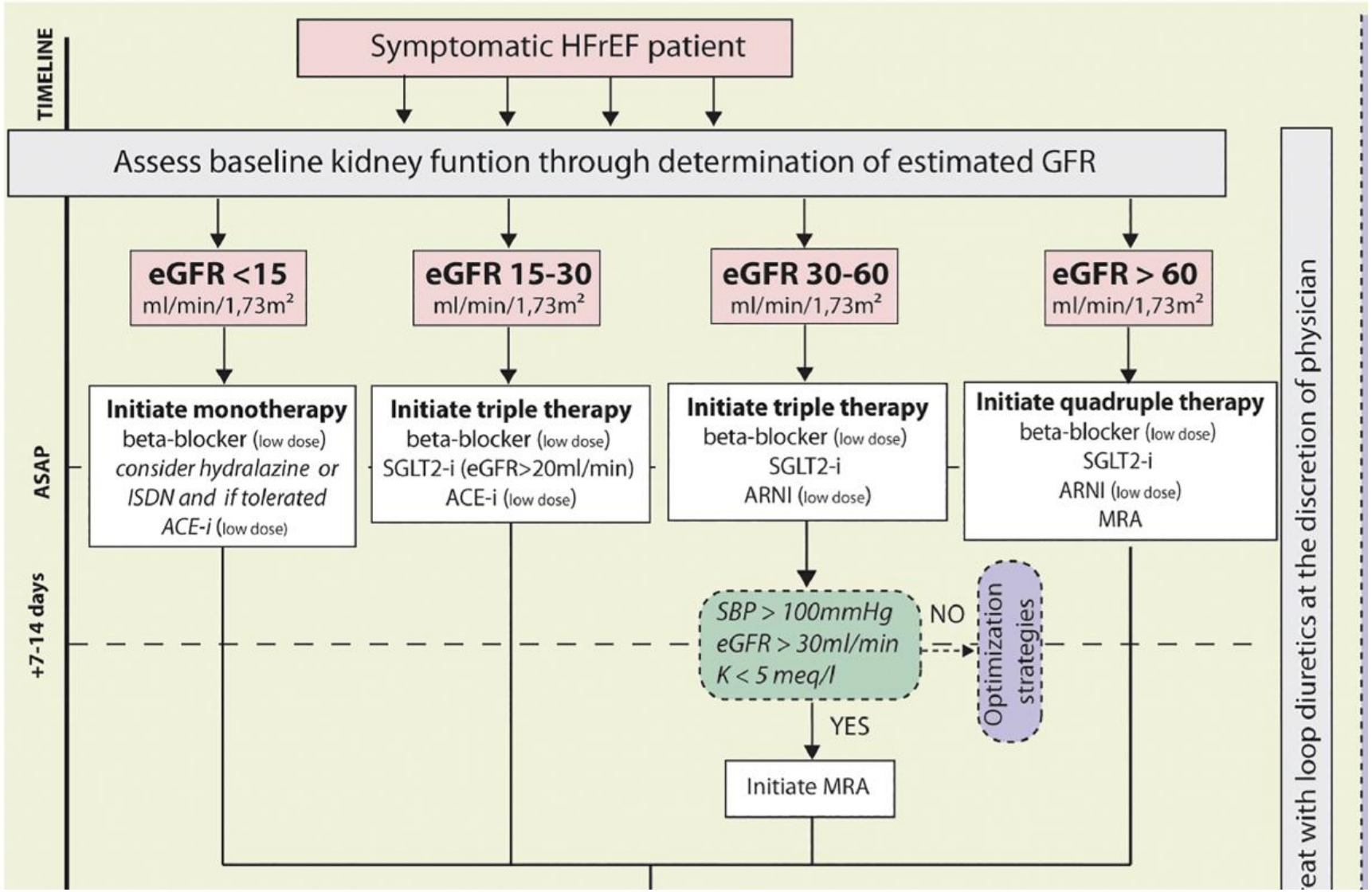
Secondary endpoints



*Morbidity-adjusted hyperkalemia-related outcomes were tested in a hierarchical manner with the following sequence: cardiovascular death, cardiovascular hospitalization, total hyperkalemia events >6.5 mmol/L, >6.0–6.5 mmol/L, and >5.0–6.0 mmol/L

Poor/worsening renal function

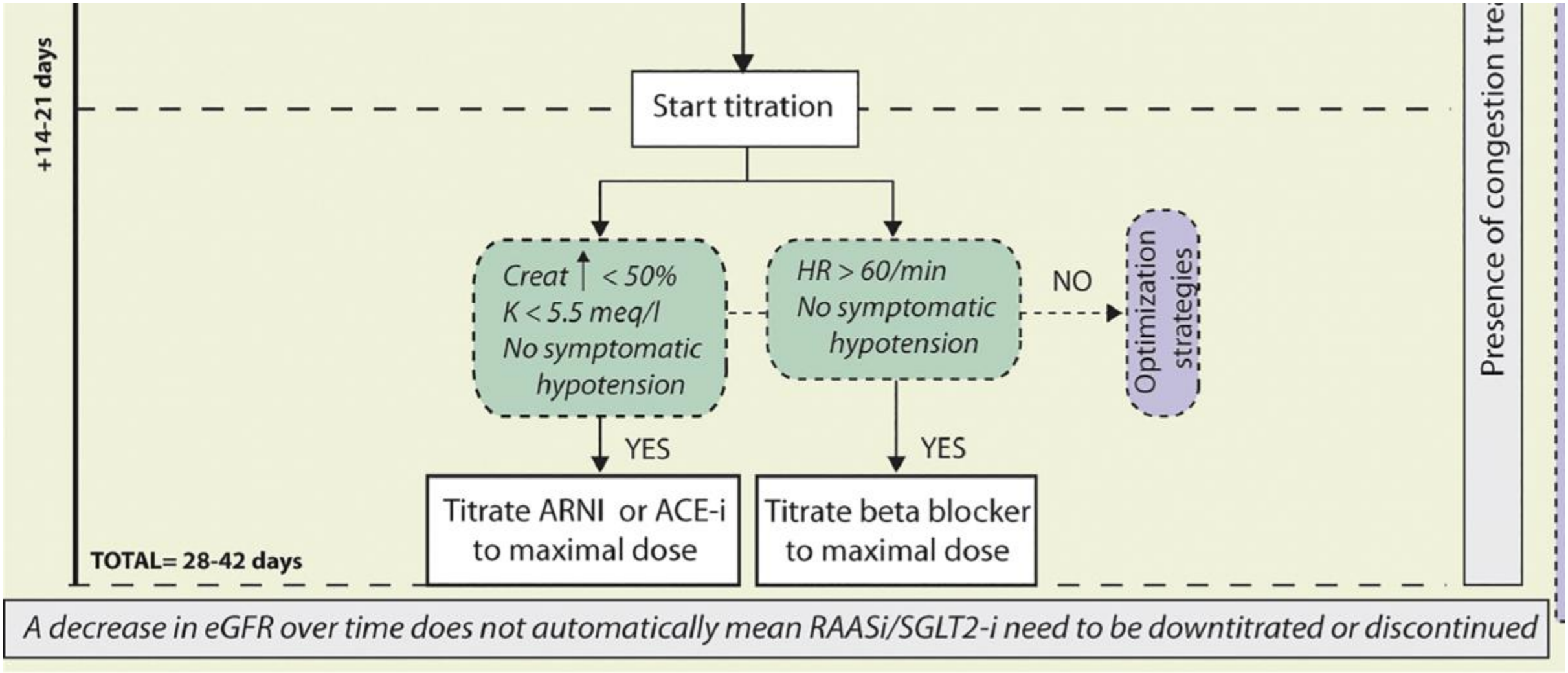
- **Pseudo WRF**: ↓ in eGFR with maintained decongestion (no adverse prognostic implications).
- Continue decongestion until dry.
- Monitor renal function and electrolytes.



Mullens W et al. European Journal of Heart Failure (2020) 22, 584–603

Mullens W et al. European Journal of Heart Failure (2022) 24, 603–619

Poor/worsening renal function



Mullens W et al. European Journal of Heart Failure (2022) 24, 603–619

ESC European Society of Cardiology

European Journal of Heart Failure (2024) **26**, 2487–2501
doi:10.1002/ejhf.3445

RESEARCH ARTICLE

Heart failure in Europe: Guideline-directed medical therapy use and decision making in chronic and acute, pre-existing and de novo, heart failure with reduced, mildly reduced, and preserved ejection fraction – the ESC EORP Heart Failure III Registry

Lars H. Lund[1,2]*, Maria Generosa Crespo-Leiro[3,4,5], Cécile Laroche[6], Diana Zaliaduonyte[7,8], Aly M. Saad[9], Candida Fonseca[10,11], Jelena Čelutkienė[12,13], Marija Zdravkovic[14,15,16], Agata M. Bielecka-Dabrowa[17,18], Piergiuseppe Agostoni[19,20], Robert G. Xuereb[21], Kseniya V. Neronova[22], Malgorzata Lelonek[23], Yuksel Cavusoglu[24], Barnabas Gellen[25], Magdy Abdelhamid[26], Naima Hammoudi[27], Stefan D. Anker[28,29,30,31], Ovidiu Chioncel[32,33], Gerasimos Filippatos[34,35], Mitja Lainscak[36,37], Theresa A. McDonagh[38], Alexandre Mebazaa[39], Massimo Piepoli[40,41], Frank Ruschitzka[42,43], Petar M. Seferović[44,45], Gianluigi Savarese[1,2], Marco Metra[46], Giuseppe M.C. Rosano[47,48,49], and Aldo P. Maggioni[50], for the ESC EORP HF III National Leaders and Investigators†

Real-world underutilisation of GDMT is a global problem

Navigating between Scylla and Charybdis: challenges and strategies for implementing guideline-directed medical therapy in heart failure with reduced ejection fraction

Petar M. Seferović[1,2]*, Marija Polovina[1,3], Christopher Adlbrecht[4], Jan Bělohlávek[5], Ovidiu Chioncel[6,7], Eva Goncalvesová[8], Ivan Milinković[1,3], Avishay Grupper[9], Róbert Halmosi[10], Ginta Kamzola[11], Konstantinos C. Koskinas[12], Yuri Lopatin[13], Alexander Parkhomenko[14], Pentti Põder[15], Arsen D. Ristić[1,3], Gintarė Šakalytė[16], Matias Trbušić[17], Meiramgul Tundybayeva[18], Bojan Vrtovec[19], Yoto T. Yotov[20,21], Davor Miličić[17], Piotr Ponikowski[22], Marco Metra[23], Giuseppe Rosano[24], and Andrew J.S. Coats[25]

- Registry data from different parts of the world suggest that **between 10% and 60%** of eligible patients do not receive one or more of the four pillars.
- Patients receiving medications are often **underdosed.**

Registry/period of data collection	No. of patients/patient characteristics	LVEF (%)	Age and comorbidities (%)	Therapy (%)	≥50% of target doses (%)
QUALIFY 2013–2014	6118/CHF	33 ± 10.8	Age 63.2 ± 12.6/78 HTA (64.4) DM (34.4) CAD (56.8) CKD (17.8)	ACEI (65.2) ARB (22.0) BB (86.5) MRA (69.2)	ACEI (72.4) ARB (49.5) BB (51.4) MRA (76.1)
ESC Heart Failure Long-Term Registry 2011–2013	12 440/ 40.5% with AHF 59.5% with CHF	AHF 38 (30–51) CHF 35 (28–45)	AHF AHF 71 (61–79)/63.7 HTA (64.5) DM (38.9) CAD (54.0) CKD (26.4) CHF Age 66 (57–75)/72.2 HTA (58.2) DM (31.8) CAD (43.0) CKD (18.2)	ACEI (70.7) ARB (23.5) BB (92.7) MRA (67.0)	ACEI (29.3) ARB (24.1) BB (17.5) MRA (30.5)
ASIAN-HF 2012–2015	5005/CHF	27	Age 59.6 ± 13.2/77 HTA (46–56) DM (39–42) CAD (44–48) CKD (38–57)	ACEI/ARB (77) BB (79) MRA (58)	ACEI/ARB (17) BB (13) MRA (29)
CHAMP-HF 2017–2018	3518/CHF	29 ± 8	Age 66 ± 13/71 HTA (78–93.2) DM (37.6–44.5) CAD (61.1–63) CKD (16.1–42.5)	ACEI/ARB (61) BB (67) MRA (34.2)	ACEI/ARB (17) BB (28) MRA (77)

European Journal of Heart Failure (2021) 23, 1999–2007

ESC European Society of Cardiology

European Journal of Heart Failure (2024) **26**, 1278–1297
doi:10.1002/ejhf.3295

POSITION PAPER

How to tackle therapeutic inertia in heart failure with reduced ejection fraction. A scientific statement of the Heart Failure Association of the ESC

Gianluigi Savarese[1,2]*, Felix Lindberg[1], Antonio Cannata[3,4], Ovidiu Chioncel[5], Davide Stolfo[1,6], Francesca Musella[1,7], Daniela Tomasoni[1,8], Magdy Abdelhamid[9], Debasish Banerjee[10], Antoni Bayes-Genis[11], Emmanuelle Berthelot[12], Frieder Braunschweig[1,2], Andrew J.S. Coats[13], Nicolas Girerd[14], Ewa A. Jankowska[15], Loreena Hill[16], Mitja Lainscak[17], Yury Lopatin[18], Lars H. Lund[1,2], Aldo P. Maggioni[19], Brenda Moura[20], Amina Rakisheva[21], Robin Ray[22], Petar M. Seferovic[23], Hadi Skouri[24], Cristiana Vitale[22], Maurizio Volterrani[25,26], Marco Metra[8], and Giuseppe M.C. Rosano[22,27]

CLINICAL RESEARCH

Global disparities in prescription of guideline-recommended drugs for heart failure with reduced ejection fraction

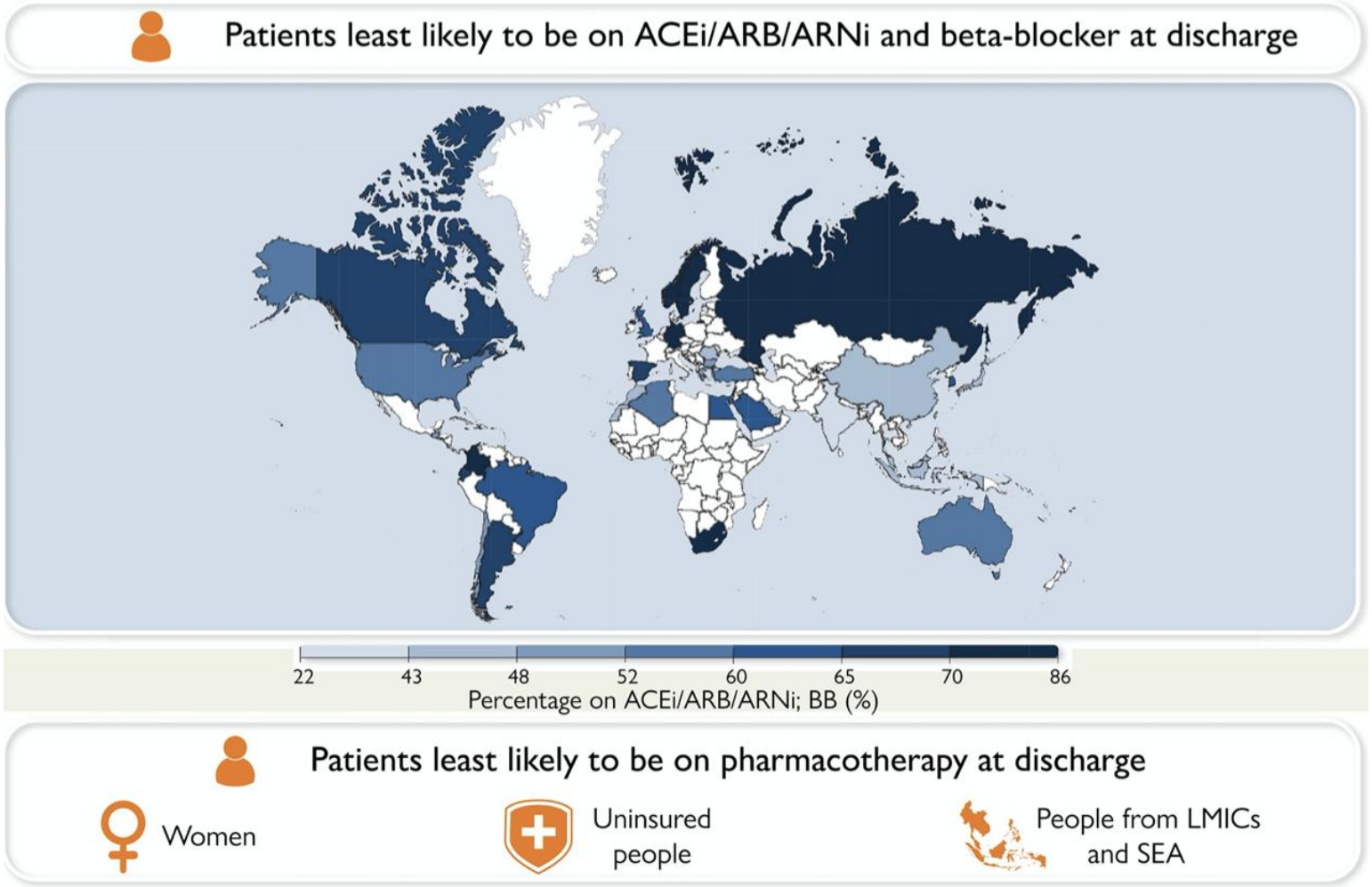
Get access >

Jasper Tromp and others

European Heart Journal, Volume 43, Issue 23, 14 June 2022, Pages 2224–2234,

Article highlight:

REPORT-HF study: Only ~37% of patients with HFrEF were discharged with at least 3 HF medications. Patients in LMICs were less likely to receive GDMT at target doses.



ESC European Society of Cardiology
European Journal of Heart Failure (2023) 25, 1507–1525
doi:10.1002/ejhf.2994
REVIEW ARTICLE

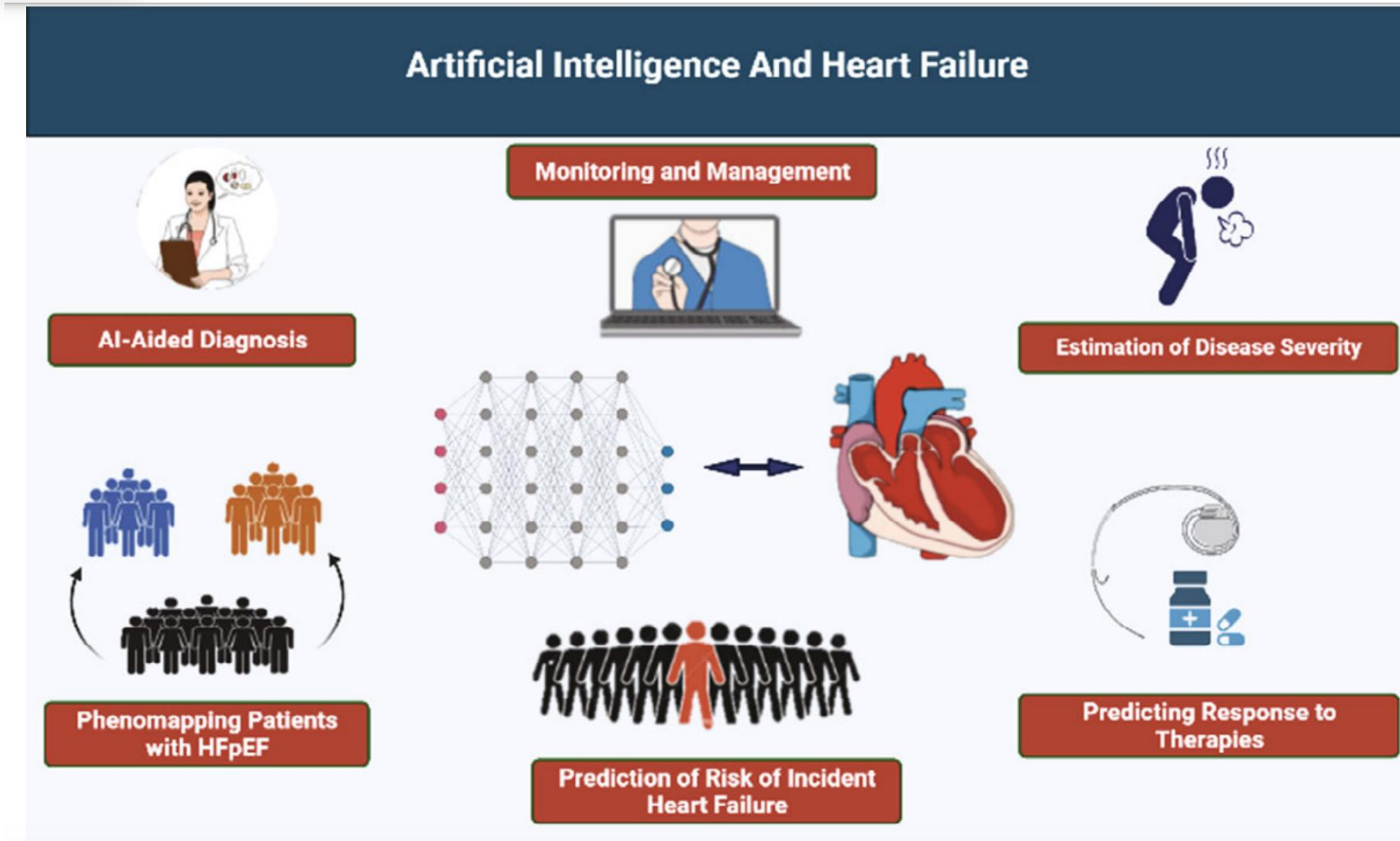
Artificial intelligence and heart failure: A state-of-the-art review

Muhammad Shahzeb Khan[1]*, Muhammad Sameer Arshad[2], Stephen J. Greene[1,3], Harriette G.C. Van Spall[4], Ambarish Pandey[5,6], Sreekanth Vemulapalli[1,3], Eric Perakslis[3], and Javed Butler[7,8]*

AI in risk assessment and management of HF

AI algorithms can facilitate clinical decision making to overcome challenges:

- **Risk prediction of incident HF.**
- **AI-aided diagnosis.**
- **Phenomapping.**
- **Estimation of disease severity.**
- **Predicting therapeutic response.**
- **Monitoring and management.**



Heart failure: Future perspectives in precision medicine

- Individual HF biology
- a. genetics
- b. pharmacogenomics
- c. proteomics

Combined with information produced by machine learning of clinical data

Can be used to guide precision treatment of heart failure

a Genetics

Heart failure and myocardial structure GWAS

Upstream contributors to coronary artery disease or atrial fibrillation
- *PITX2–FAM241A*
- *CDKN2B–AS1*
- *LPA*

Sarcomeric genes
- *TTN*
- *TTNT2*
- *ACTN2*

Developmental genes
- *TBX3*
- *HAND1*
- *GOSR1*
- *MTSS1*

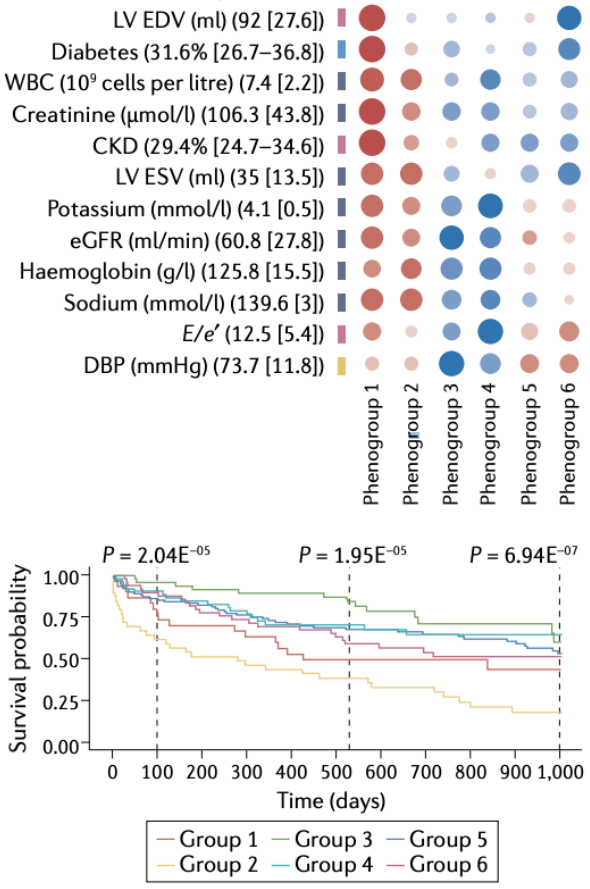
Cell signalling and survival genes
- *PLN*
- *BAG3*
- *CDKN1A*
- *KLHL3*

b Pharmacogenomics
- Angiotensin receptors
- β-Adrenergic receptors
- G-protein-coupled receptor kinases
- Orexin

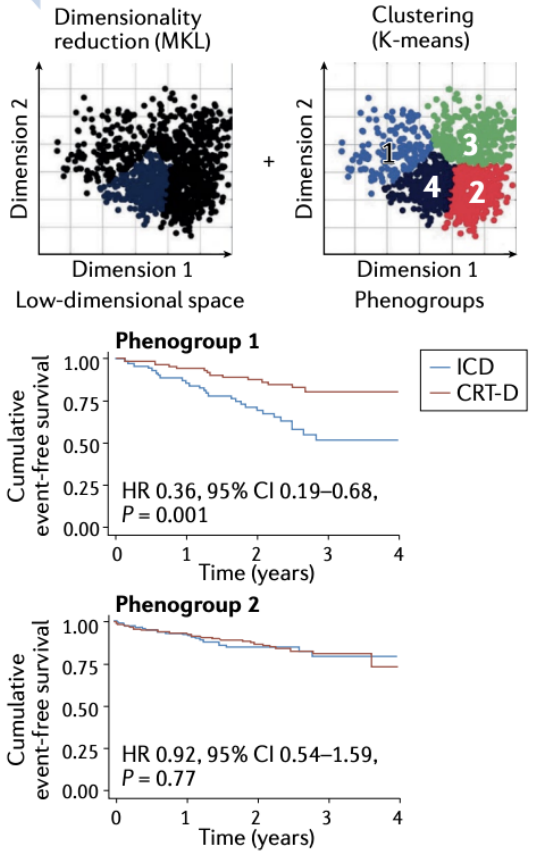
c Proteomics
- Inflammation
- Matrix remodelling
- Coagulation system
- Oxidative stress
- Angiogenesis

d Machine learning

Electronic health record data and proteomic data



Expanded machine learning to guide precision treatment for heart failure
- Polygenic risk
- Pharmacogenomic background
- Proteomic signature
- Electronic health record data

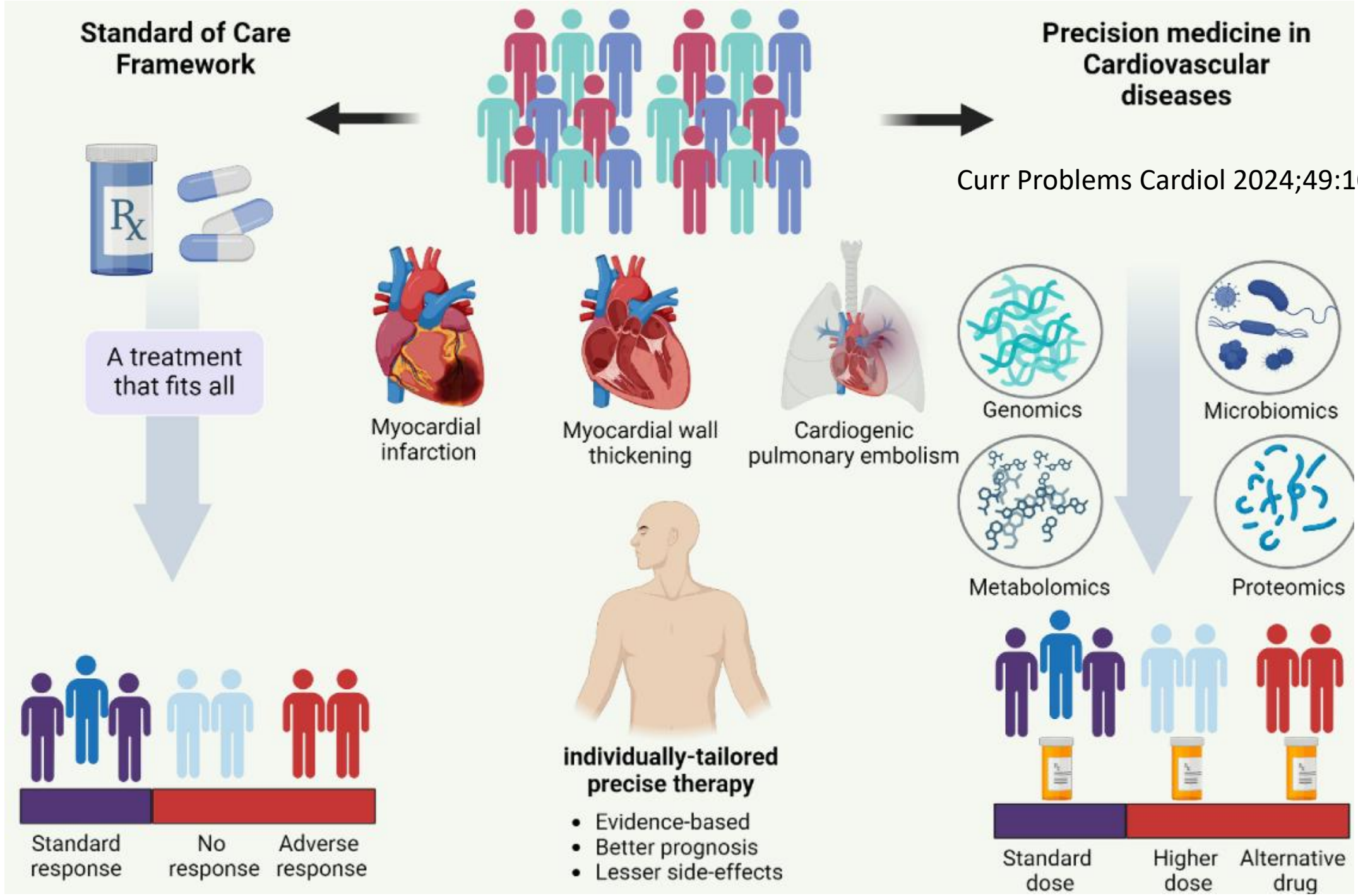


Differential response to cardiac resynchronization therapy determined by machine learning-based phenomapping

↓

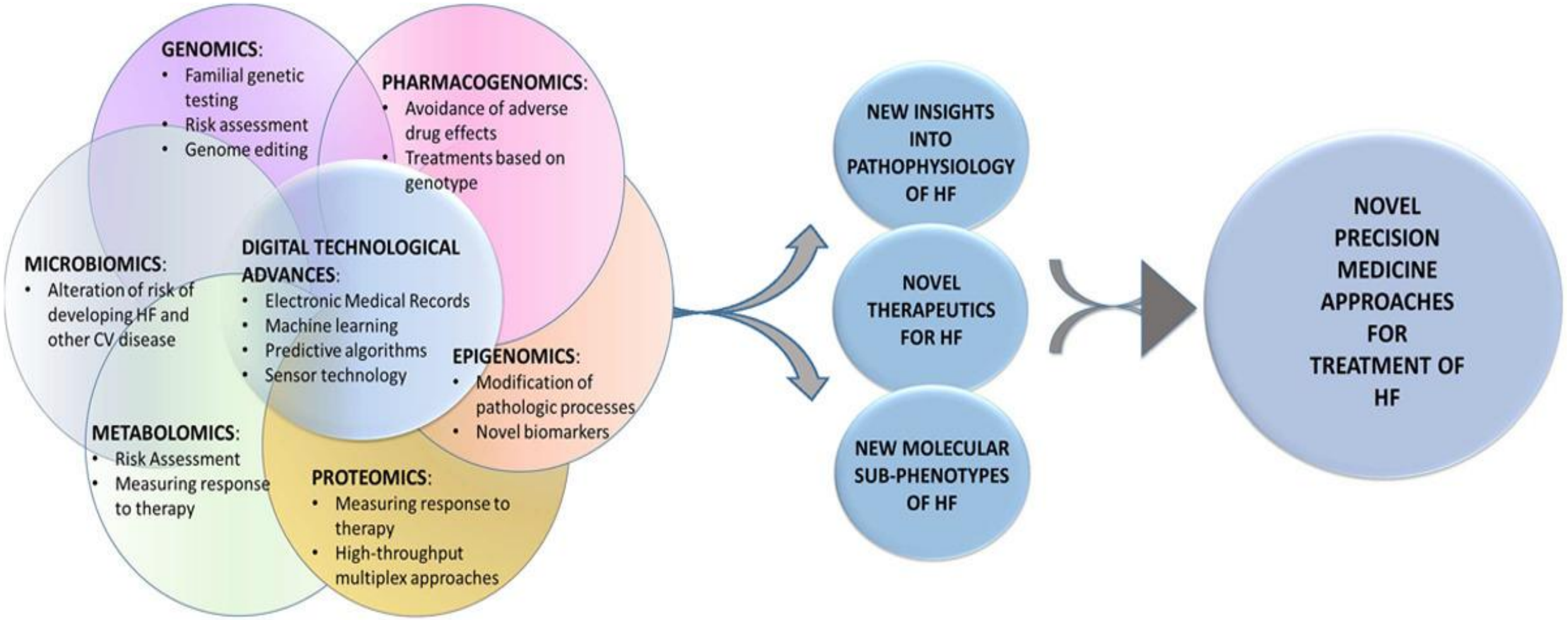
Precision medicine targeted to individual patients by selecting therapies and interventions based on causal biology

Weldy, S, Ashley A. Towards precision medicine in heart failure.
Nature Reviews Cardiology. (2021) doi:10.1038/s41569-021-00566-9


Standard of Care Framework
Precision medicine in Cardiovascular diseases
Curr Problems Cardiol 2024;49:102470
Rx
A treatment that fits all
Myocardial infarction
Myocardial wall thickening
Cardiogenic pulmonary embolism
Genomics
Microbiomics
Metabolomics
Proteomics
Standard response
No response
Adverse response
individually-tailored precise therapy
Evidence-based
Better prognosis
Lesser side-effects
Standard dose
Higher dose
Alternative drug

Precision medicine in HF: From AI to clinical application

Combining advances in basic sciences, pharmacology, artificial intelligence and digital technologies will provide a more nuanced perspective of HF pathophysiology and therapeutic targets in HF



Cresci S et al. Circulation: Genomic and Precision Medicine. 2019;12:e000058

STRATIFYHF: European megaproject in HF prevention

STRATIFYHF

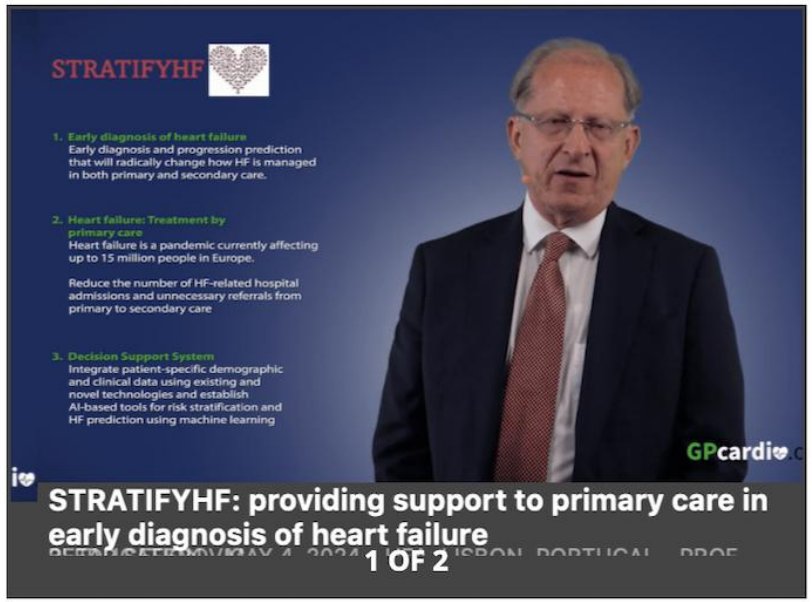
The EPCCS partners in the European Union co-funded research programme STRATIFYHF which aims to develop and clinically validate a truly innovative AI-based Decision Support System (STRATIFYHF) for predicting risk of HF, facilitating its early diagnosis and progression prediction that will radically change how HF is managed in both primary and secondary care

RECENT

The STRATIFYHF Research and Innovation Action
3' EDUCATION - MAY 6, 2024 - PROF. DJORDJE JAKOVLJEVIC

STRATIFYHF: providing support to primary care in early diagnosis of heart failure
3' EDUCATION - MAY 4, 2024 - HFA, LISBON, PORTUGAL - PROF. PETAR SEFEROVIC

STRATIFY-HF A European collaboration to develop an AI based support system for risk stratification and early detection of heart failure
APR. 2, 2024



The STRATIFYHF Research and Innovation Action

3' EDUCATION - MAY 6, 2024 - PROF. DJORDJE JAKOVLJEVIC

STRATIFYHF: providing support to primary care in early diagnosis of heart failure

STRATIFYHF

Artificial intelligence-based decision support system for risk stratification and early detection of heart failure in primary and secondary care

3' EDUCATION

The STRATIFYHF Research and Innovation Action
3' EDUCATION - MAY 6, 2024 - PROF. DJORDJE JAKOVLJEVIC

STRATIFYHF: providing support to primary care in early diagnosis of heart failure
3' EDUCATION - MAY 4, 2024 - HFA, LISBON, PORTUGAL - PROF. PETAR SEFEROVIC

SHOW MORE

STRATIFYHF: Project description

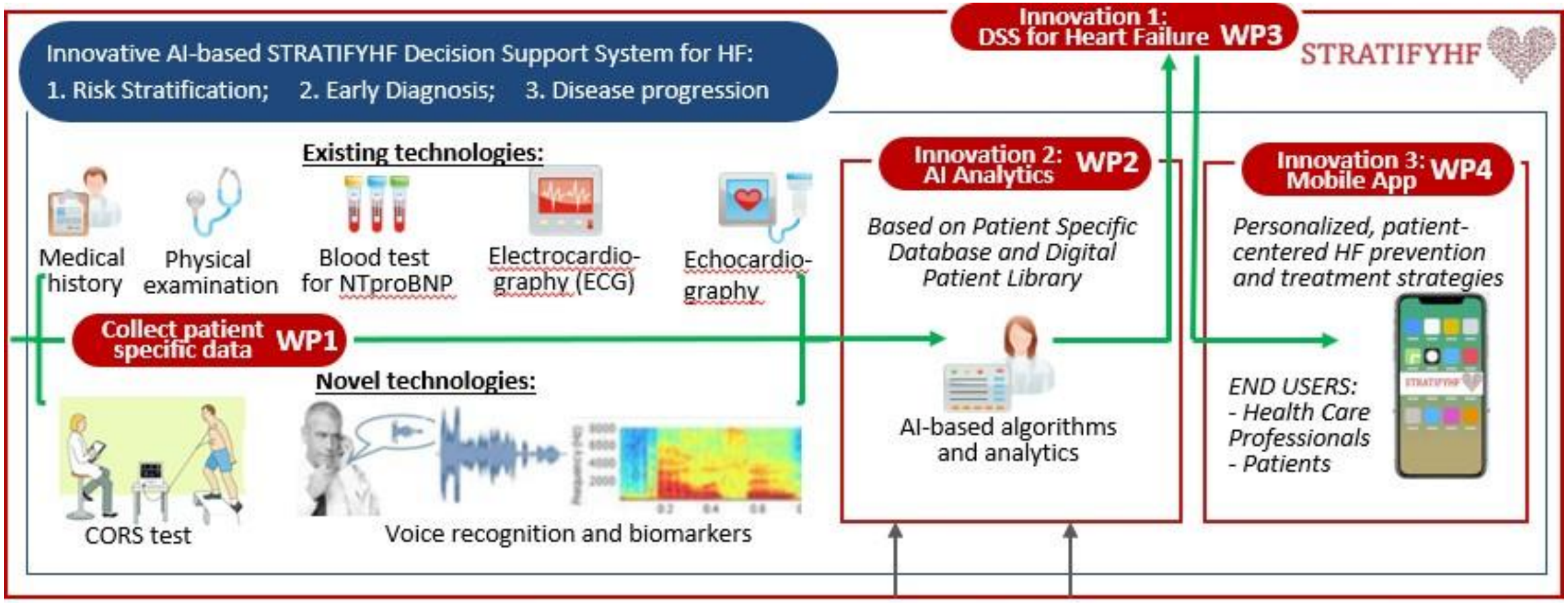


Figure 3. STRATIFYHF innovative AI-based Decisions Support System for Heart Failure

- Phase 1: Retrospective 8,000 patients
- Phase 2: Prospective 1,600 patients

BMJ Open

Clinical validation of an artificial intelligence-based decision support system for diagnosis and risk stratification of heart failure (STRATIFYHF): a protocol for a prospective, multicentre longitudinal study

Sarah Jane Charman ,[1,2] Nduka C Okwose,[3,4] Amy Groenewegen ,[5] Annamaria Del Franco ,[6] Maria Tafelmeier,[7] Andrej Preveden,[8,9] Cristina Garcia Sebastian,[10] Amy S Fuller,[3,4] David Sinclair ,[11] Duncan Edwards,[12] Anne Pauline Nelissen,[5] Petros Malitas,[13] Aikaterini Zisaki,[13] Josep Darba,[14] Zoran Bosnic,[15] Petar Vracar,[15] Fausto Barlocco,[6] Dimitris Fotiadis,[16] Prithwish Banerjee ,[17] Guy A MacGowan,[2,18] Oscar Fernandez,[2] José Zamorano,[10,19] Marta Jiménez-Blanco Bravo,[10,19] Lars S Maier,[7] Iacopo Olivotto ,[20] Frans H Rutten ,[5] Jonathan Mant ,[12] Lazar Velicki,[8,9] Petar M Seferović,[21] Nenad Filipovic,[22,23] Djordje G Jakovljevic,[1,2,3,4] STRATIFYHF investigators[1]

To cite: Charman SJ, Okwose NC, Groenewegen A, *et al*. Clinical validation of an artificial intelligence-

ESC European Society of Cardiology

European Heart Journal (2024) **45**, 4987–4989
https://doi.org/10.1093/eurheartj/ehad897

CardioPulse

Global Spotlights

The *ESC Textbook of Heart Failure*: breaking the new educational frontier

Petar M. Seferovic [1]*, Andrew J. S. Coats [2], and Gerasimos Filippatos [3]

Manuel Jimenez Prieto: Martin Charcot visits a patient, 1897

Heart Failure 2012

BELGRADE
SERBIA
19-22 MAY

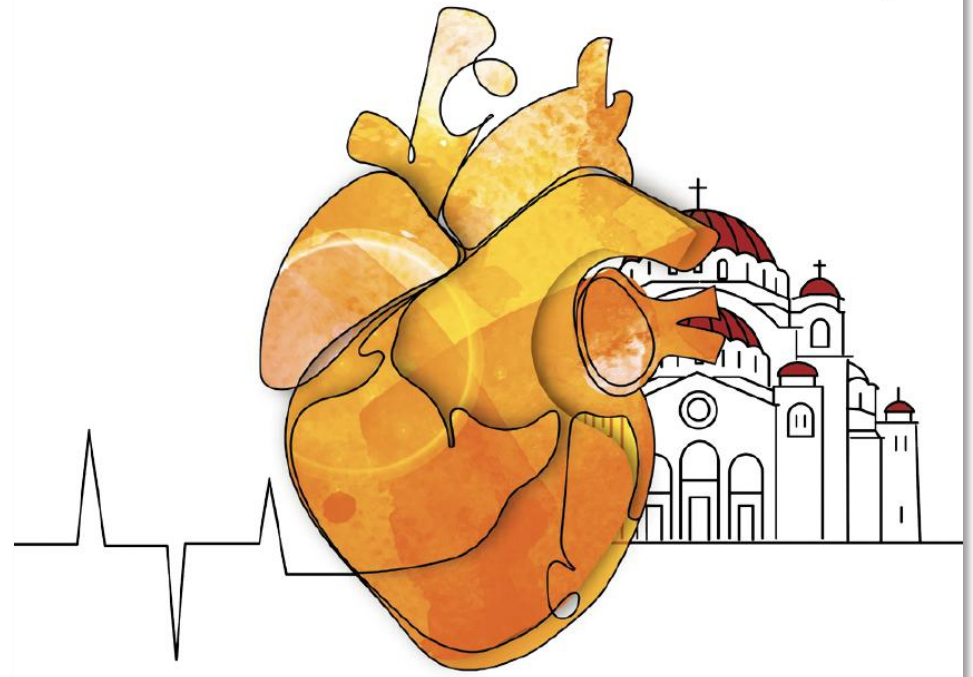
www.escardio.org/HFA

ADVANCE PROGRAMME

ISHR

HFA
Heart Failure
Association

Heart Failure
& World Congress on Acute Heart Failure
# 2025



17-20 MAY

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Annual Congress of the Heart Failure Association of the ESC

escardio.org/heartfailure
#HeartFailure2025

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