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)

Precision heart failure therapy: From Guidelines to implementation in the Eastern Europe

Academician, Serbian Academy of Sciences and Arts

Professor of Cardiology, Belgrade University School of Medicine

President, Heart failure Society of Serbia

Precision medicine in heart failure

Precision medicine:

- An innovative approach that uses information about genomic, environmental, and lifestyle information to guide decisions related to the medical management.

The goal:

- To provide a more precise approach for the prevention, diagnosis, and treatment of disease.

The challenge of individualized treatment in heart failure:

- Effect of comorbidities and etiologies vs.anatomic and hemodinamic myocardial disfunction
- Defining optimal treatment choices,
- Variability of patient's response to the treatment,
- Risk of intolerance and side effects.

National Human Genome Research Institute (n.d.) . Personalized Medicine. Bethesda: National Human Genome Research Institute.

Circulation: Genomic and Precision Medicine
Volume 12, Issue 10, October 2019
https://doi.org/10.1161/HCG.0000000000000058

American Heart Association.

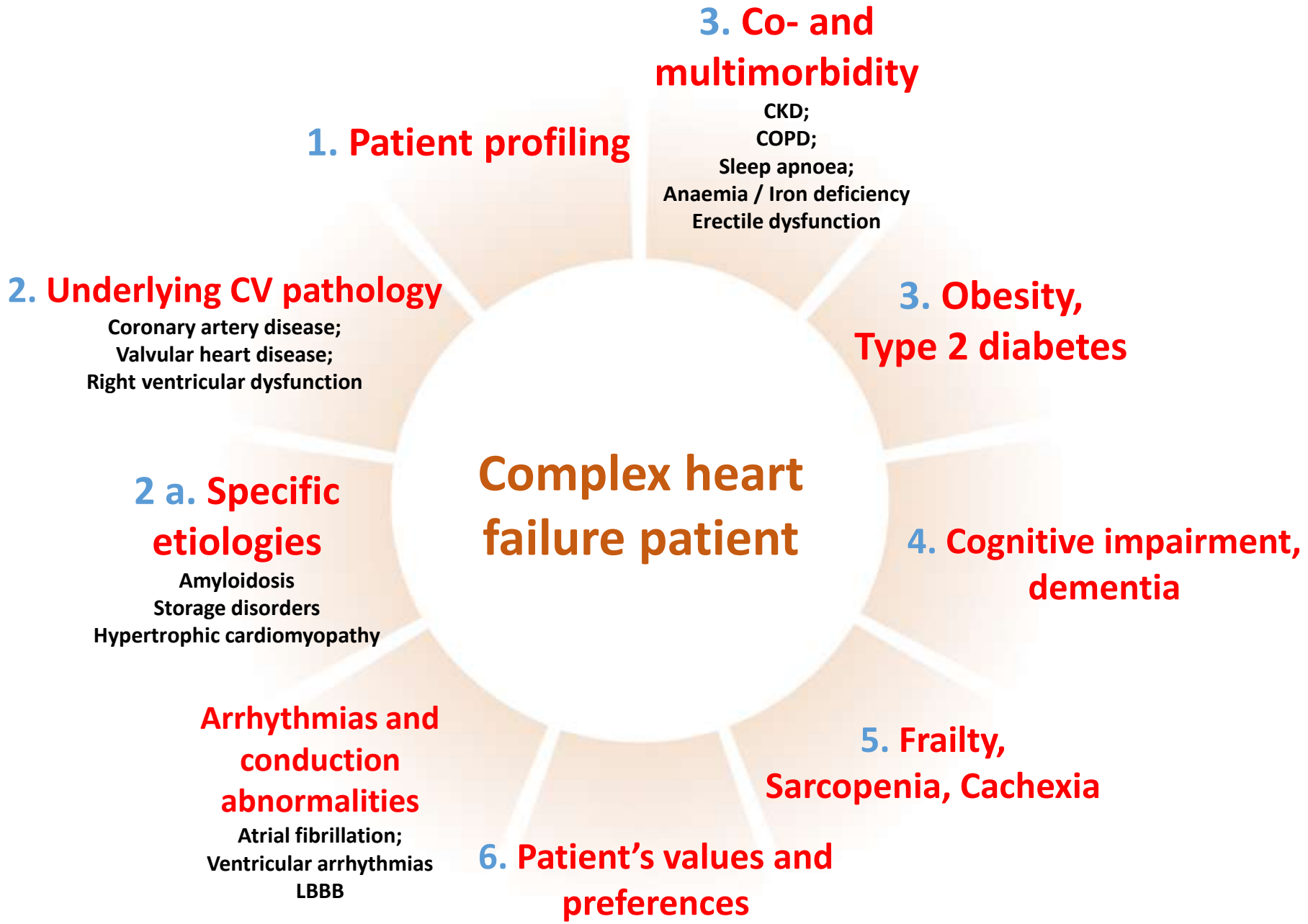
AHA SCIENTIFIC STATEMENT

Heart Failure in the Era of Precision Medicine: A Scientific Statement From the American Heart Association

Sharon Cresci, MD, FAHA, Chair, Naveen L. Pereira, MD, FAHA, Vice Chair, Ferhaan Ahmad, MD, PhD, FRCPC, FAHA, Mirnela Byku, MD, PhD, Lisa de las Fuentes, MD, MS, FAHA, David E. Lanfear, MD, MS, FAHA, Carolyn M. Reilly, PhD, RN, FAHA, Anjali T. Owens, MD, and Matthew J. Wolf, MD, PhD, FAHA

Medical care designed to optimize efficiency or therapeutic benefit for particular groups of patients, especially by using genetic or molecular profiling

Precision treatment vs complexity of heart failure



Strategies to improve treatment of complex heart failure patients

1. Patient profiling

Tailoring medical therapy to specific clinical profile

Consider: blood pressure, heart rate, atrial fibrillation, CKD, electrolyte abnormalities, residual congestion

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

2. Heart failure specific etiologies

Cardiovascular etiologies

a. Coronary artery disease

Consider secondary prevention measures & revascularisation

b. Valvular heart disease

- **Aortic stenosis:**

Consider aortic valve replacement

- **Functional mitral regurgitation:**

Consider mitral valve repair (MitraClip)

- **Tricuspid regurgitation:**

Consider tricuspid valve repair (TriClip)

c. Hypertrophic obstructive cardiomyopathy

Consider septal reduction / mavacamten

Systemic etiologies

AL amyloidosis

Haematological treatment

TTR amyloidosis

Tafamidis, Patisiran

Haemochromatosis

Therapeutic phlebotomy / iron chelating agents

Storage disorders

Enzyme replacement therapy

3. Comorbidities

Common comorbidities in heart failure that can affect the use of GDMT

Comorbidity	GDMT	Precaution	Comment
Coronary artery disease and angina	✓		Beta-blockers and ivabradine may help control symptoms
Diabetes	✓		GDMT have shown similar benefits in diabetic patients
Lung disease		Asthma is a relative contraindication to beta-blocker; starting with low doses of cardio-selective beta-blocker may allow its use	Beta-blockers can be given in COPD
Depression	✓		Depression is associated with low adherence to medication
Erectile dysfunction	✓		Thiazides, spironolactone and beta-blockers (nebivolol preferred) may aggravate erectile dysfunction
Iron deficiency/anaemia	✓		
Kidney dysfunction		ACEi, ARB, ARNI, MRA may have some limitations (see text)	Diuretics may need higher doses to be effective
Cachexia		ACEi, ARB, ARNI should be up-titrated carefully because of orthostatic hypotension	

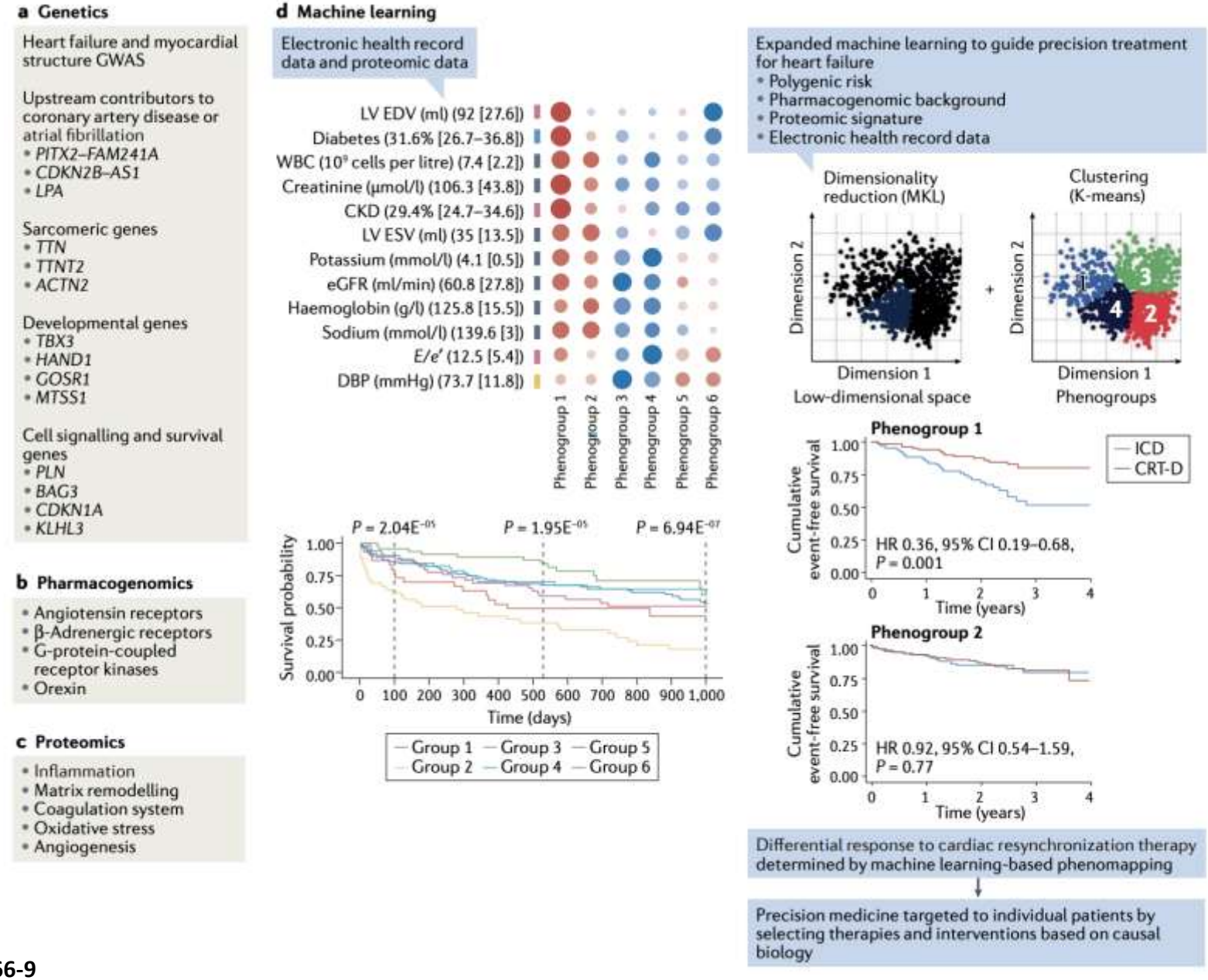
Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. Rosano G et al. European Journal of Heart Failure (2021) 23, 872–881

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



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

Circulation: Genomic and Precision Medicine

ORIGINAL ARTICLES

Genetic Association Analyses Highlight *IL6*, *ALPL*, and *NAV1* As 3 New Susceptibility Genes Underlying Calcific Aortic Valve Stenosis

Integration of Large-Scale Genomic Data Sources With Evolutionary History Reveals Novel Genetic Loci for Congenital Heart Disease

CLINICAL LETTER

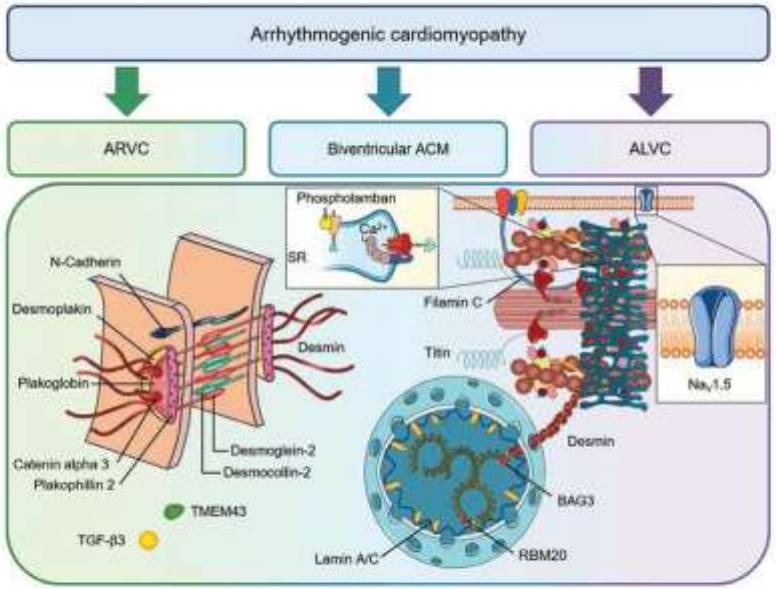
Pathological Overlap of Arrhythmogenic Right Ventricular Cardiomyopathy and Cardiac Sarcoidosis

PERSPECTIVE

Revisiting the Approach to Diagnosis of Arrhythmogenic Cardiomyopathy: Stick to the Arrhythmia Criterion!

AHA SCIENTIFIC STATEMENT

Heart Failure in the Era of Precision Medicine: A Scientific Statement From the American Heart Association



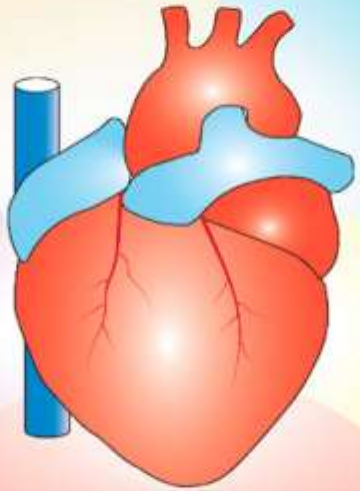
American Heart Association.

Volume 12, Number 10, October 2019

ISSN 2574-8300
https://www.ahajournals.org/journal/circgen

PROTEOMICS
- Risk Assessment
- Risk Stratification
- Novel diagnostic biomarkers
- Guided Therapy

METABOLOMICS
- Measure response to Perturbations
- Improved understanding of heart physiology



ARTIFICIAL INTELLIGENCE
- Multimodal and multidimensional omics
- Enhanced diagnostic and therapeutic modalities

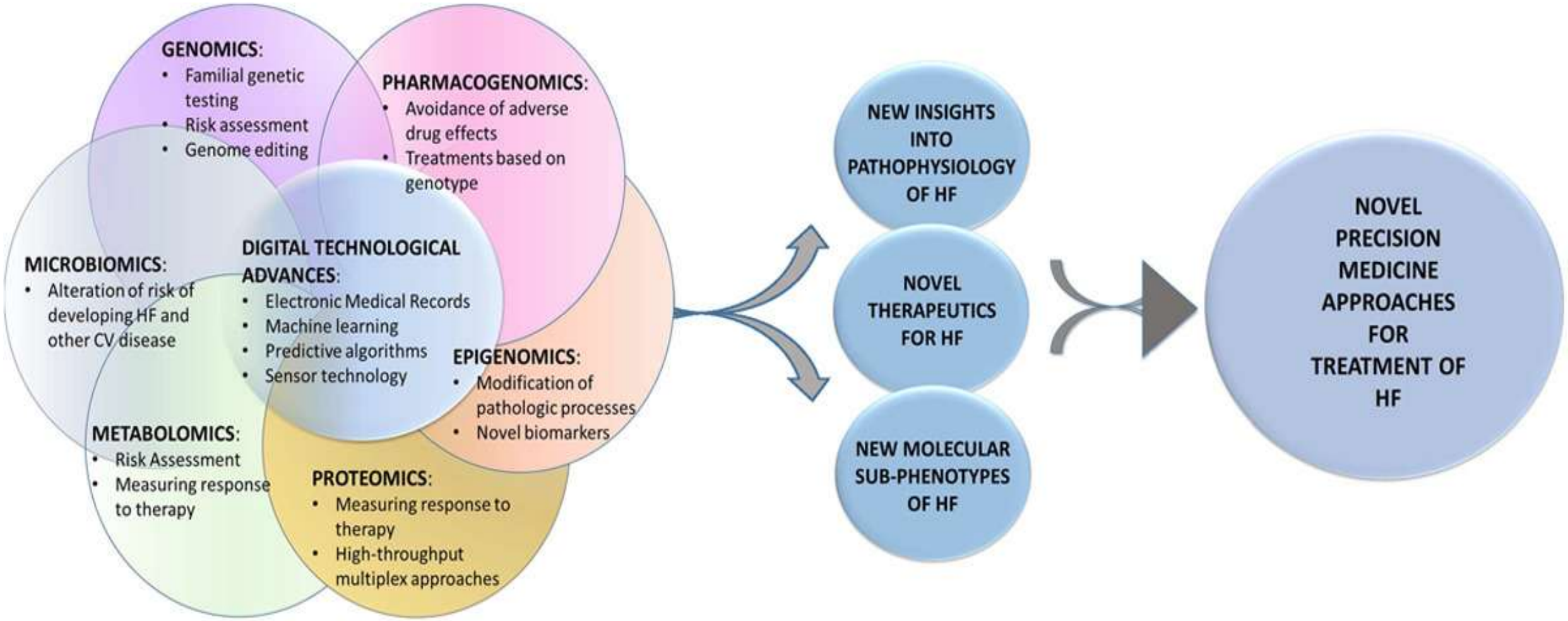
MICROBIOMICS
- Prognostic markers
- Risk assessment
- Integrated Medicine

GENOMICS
- Risk assessment and stratification
- Gene-targetted therapy
- Genetic variants Identification

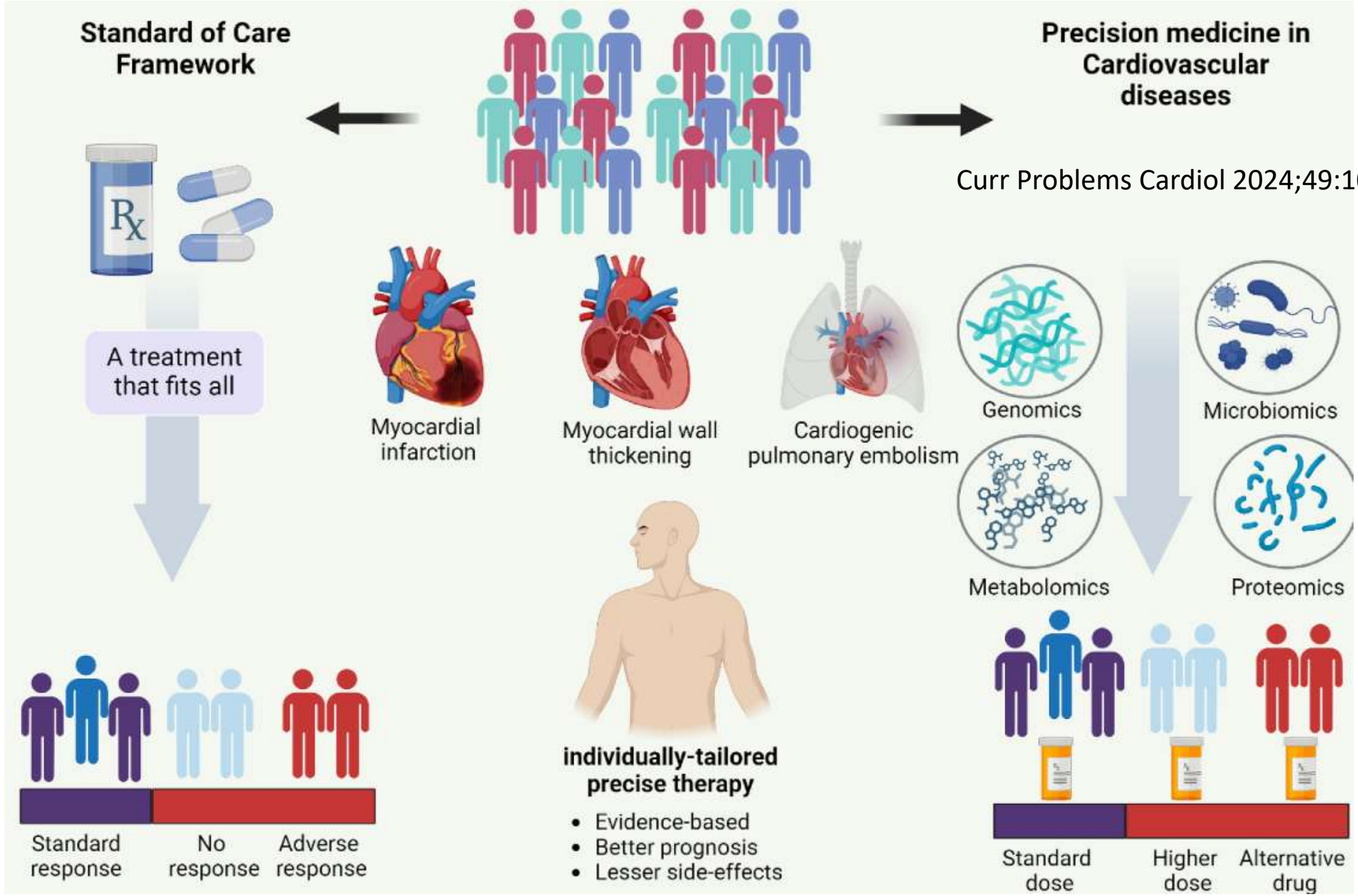
Sethi Y, et al. J Clin Med. 2023; 12(5):1799.

Future perspectives in precision medicine

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


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

European HF Survey: overview

- 43 ESC member countries, >900 million population.
- Collaborative effort, ESC/HFA and NHFS.
- National data sources.
- Standardized data reporting (2013 European Standard Population).
- Data collection for 2019.

Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025

HF epidemiology across the 42 ESC member countries

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.3710

RESEARCH ARTICLE

Insights into the European heart failure epidemiology

Petar M. Seferović[1,2*], Marija Polovina[1,3], Gianluigi Savarese[4,5], Ivan Milinković[1,3], Dejana Stanisavljević[1,4], Lars Lund[5,6], Ovidiu Chioncel[7], Magdy Abdelhamid[8], Yuri Lopatin[9], Stefan Störk[10], Manuel Anguita Sanchez[11], Massimo Piepoli[12,13], Aldo P. Maggioni[14], Ewa Jankowska[15], Antoni Bayes-Genis[16], Alain Cohen Solal[17], Arsen Ristić[1,3], Mariya Tokmakova[18], Mehmet Birhan Yilmaz[19], Hadi Skouri[20], Davor Miličić[21], Offer Amir[22], Amina Rakisheva[23], Gerasimos Filippatos[24], Giuseppe Rosano[25], Marco Metra[26], and Andrew J. Coats[27]

2019 HFA Atlas vs 2025 European HF Survey

Heart failure incidence

Median incidence 2019:

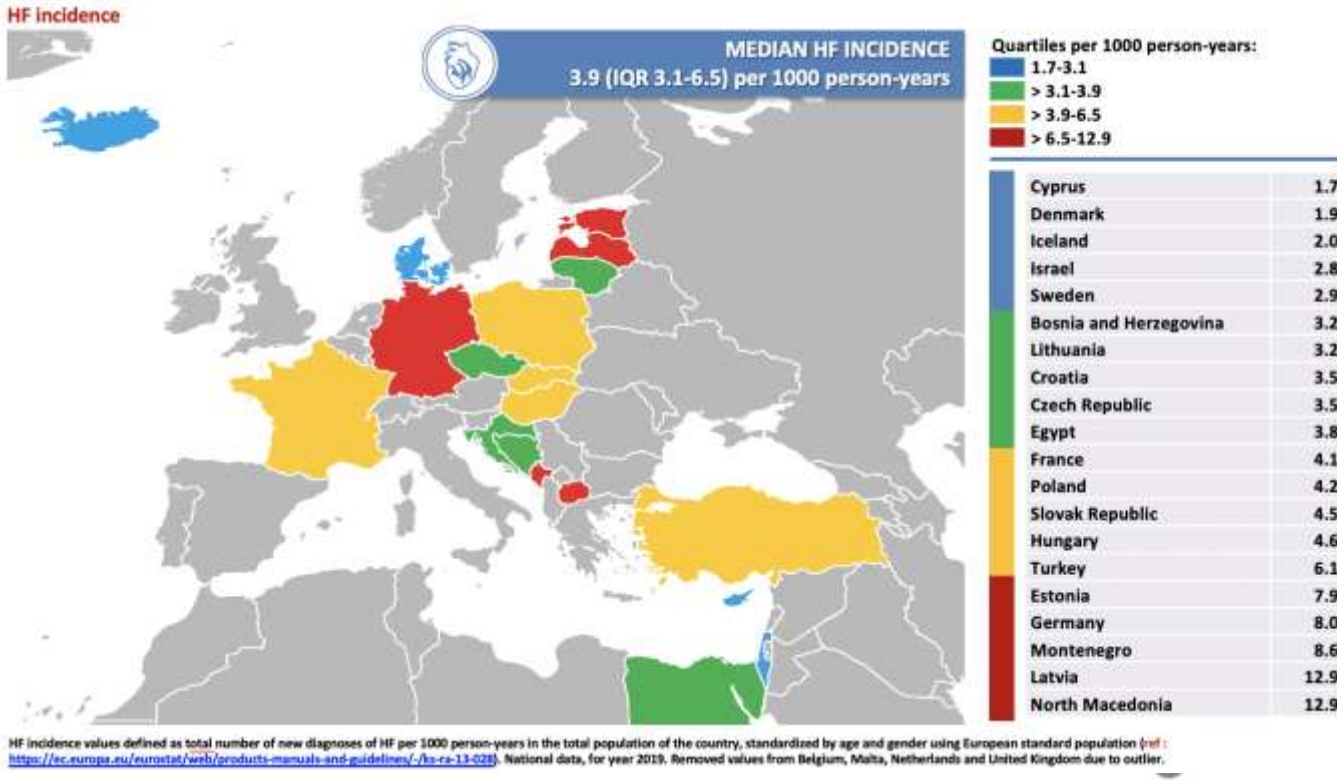
3.2 new cases per 1000 PY

Incidence: number of new cases of heart failure per 1000 person-years. **Data in blue letters derived from**: national statistics, governmental and/or ministry of health documents and prospective national registries/surveys; **Data in orange letters derived from**: publications based on defined populations (e.g. regional registries/surveys).

Acute Heart Failure 2025

Median incidence 2025:

3.9 new cases per 1000 PY



HF incidence values defined as total number of new diagnoses of HF per 1000 person-years in the total population of the country, standardized by age and gender using European standard population (ref : https://ec.europa.eu/eurostat/web/products-manuals-and-guidelines/-/ks-ra-13-028). National data, for year 2019. Removed values from Belgium, Malta, Netherlands and United Kingdom due to outlier.

Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025

2019 HFA Atlas vs 2025 European HF Survey

Heart failure prevalence

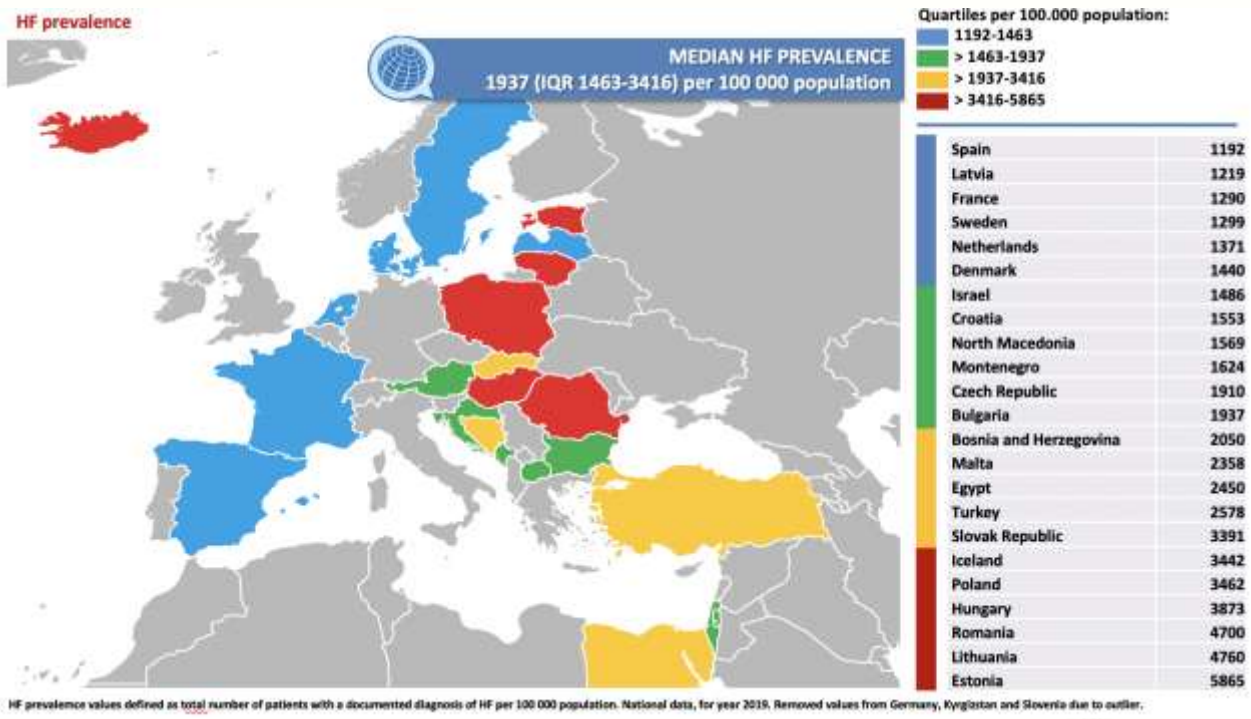
Median prevalence 2019:

1.7% total population

Seferović P et al. Eur J Heart Fail.2021 Jun;23(6):906-914

Median prevalence 2025:

1.9% total population



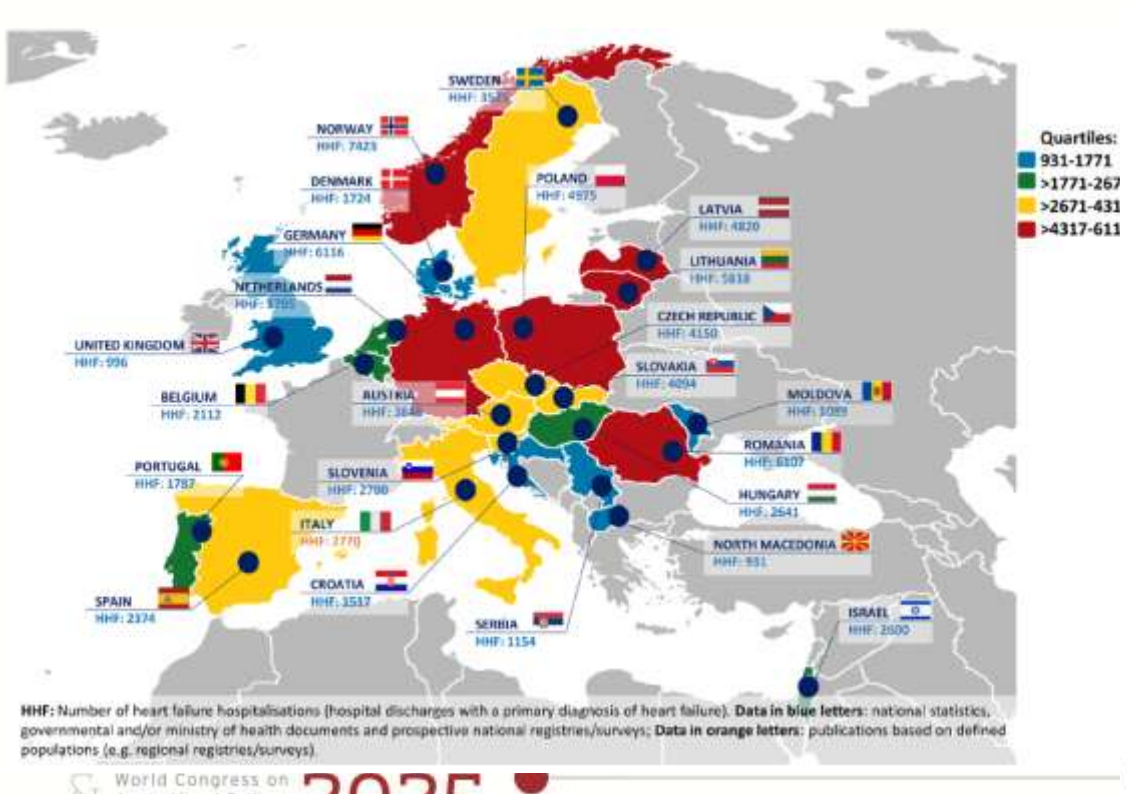
Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025

2019 HFA Atlas vs 2025 European HF Survey

Hospitalisations for heart failure

Median No of hospitalisations 2019:

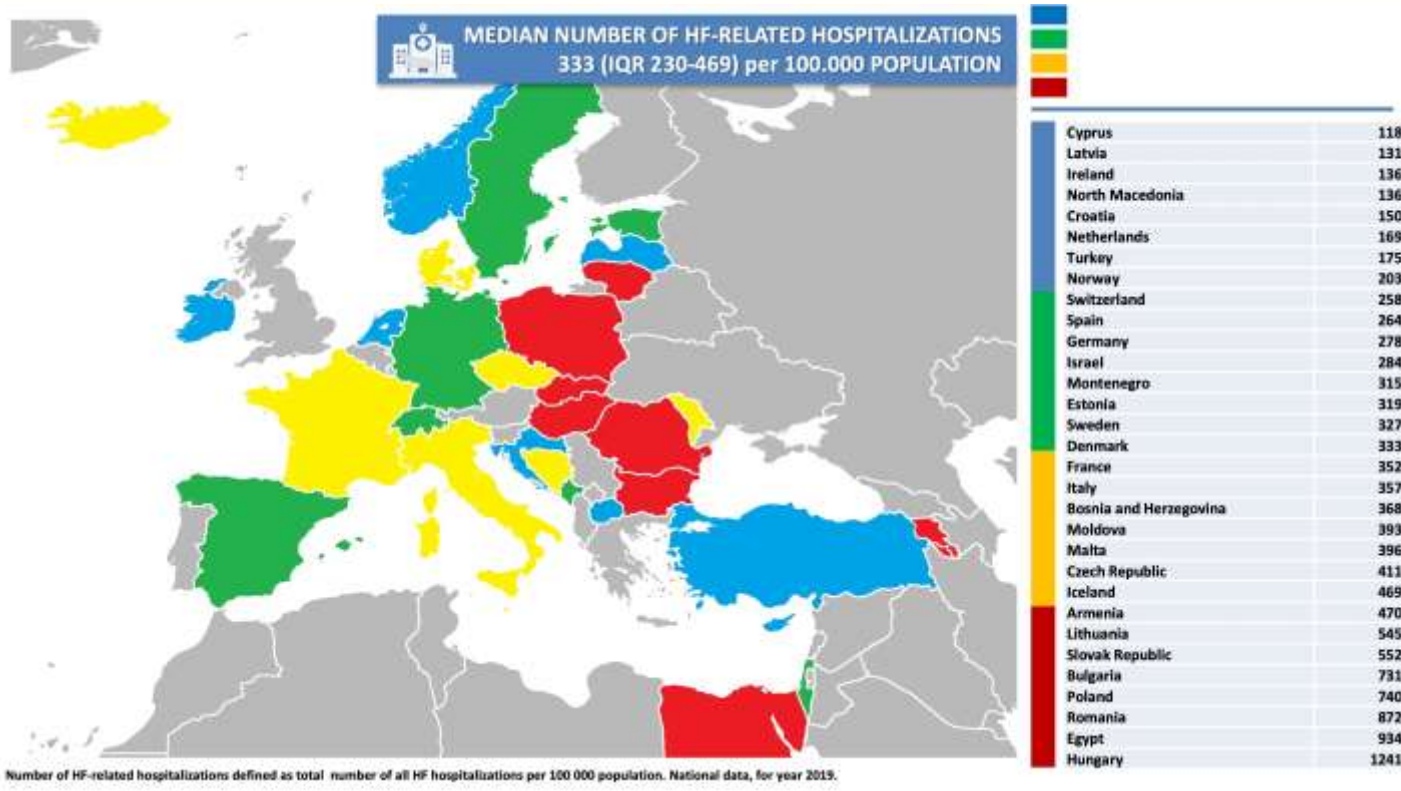
267 per 100,000 population per year



Seferović P et al. Eur J Heart Fail.2021 Jun;23(6):906-914

Median No of hospitalisation 2025:

333 per 100,000 population per year



Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025

World Congress on Acute Heart Failure 2025

Dedicated resources, devices and medications for heart failure

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.3691

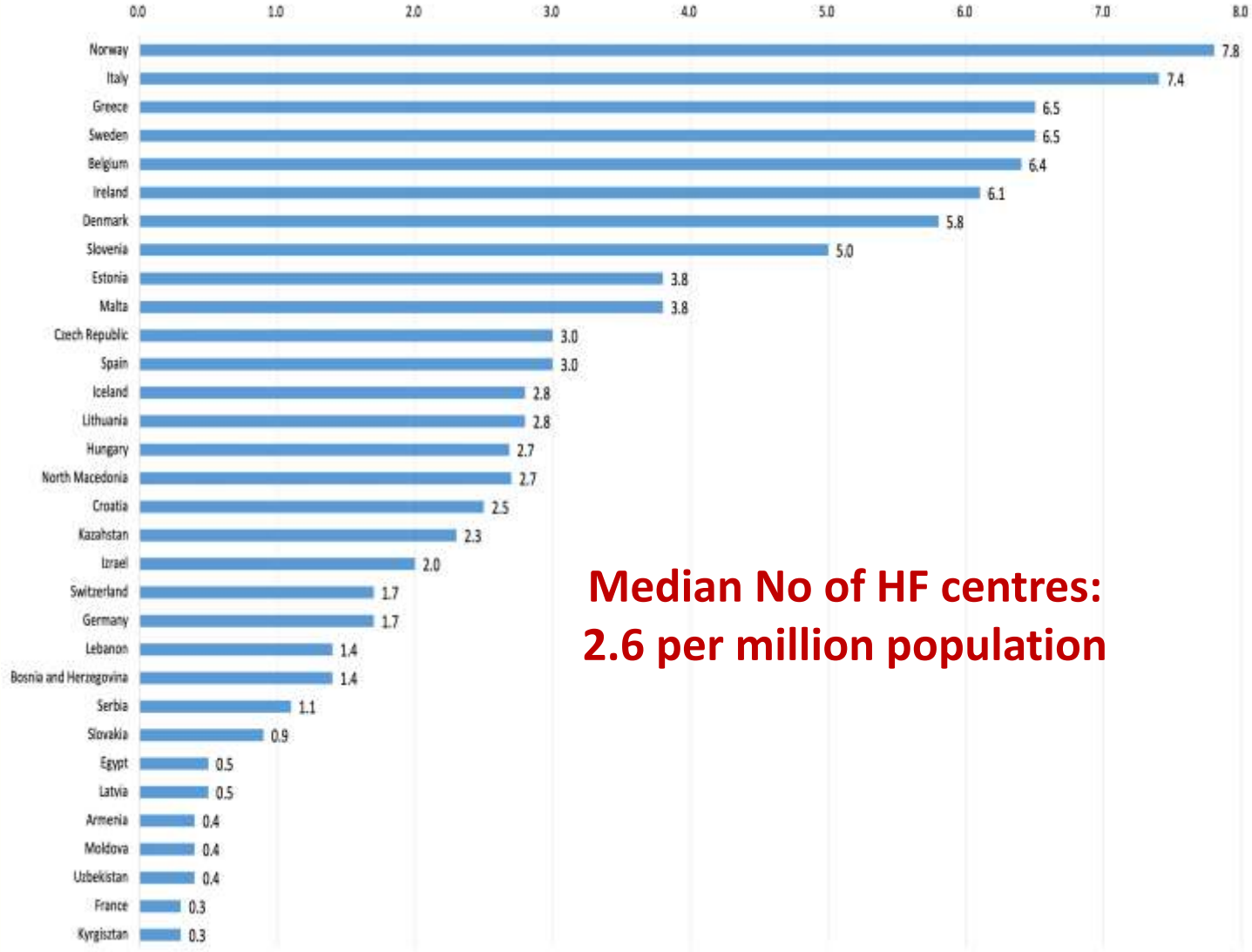
RESEARCH ARTICLE

The European heart failure management resources, treatment reimbursement and activities of professional and patient organizations

Petar M. Seferović[1,2*], Marija Polovina[1,3], Gianluigi Savarese[4,5], Ivan Milinković[1,3], Lars Lund[4,5], Ovidiu Chioncel[6], Magdy Abdelhamid[7], Yuri Lopatin[8], Stefan Störk[9,10], Manuel Anguita Sanchez[11], Massimo Piepoli[12,13], Aldo P. Maggioni[14], Ewa Jankowska[15], Antoni Bayes-Genis[16], Alain Cohen Solal[17], Arsen Ristić[1,3], Mariya Tokmakova[18], Mehmet Birhan Yilmaz[19], Hadi Skouri[20], Davor Miličić[21], Offer Amir[22], Amina Rakisheva[23], Gerasimos Filippatos[24], Giuseppe Rosano[25], Marco Metra[26], and Andrew J. Coats[27]

HF centres and diagnostic capacities

- Improved access to specialised HF centres.
- Improvement in ED and in-hospital availability of NP testing, CMR, CTCA, CPET.
- Low availability of NP testing in out-of-hospital/primary care setting
- Modest availability of EMB.

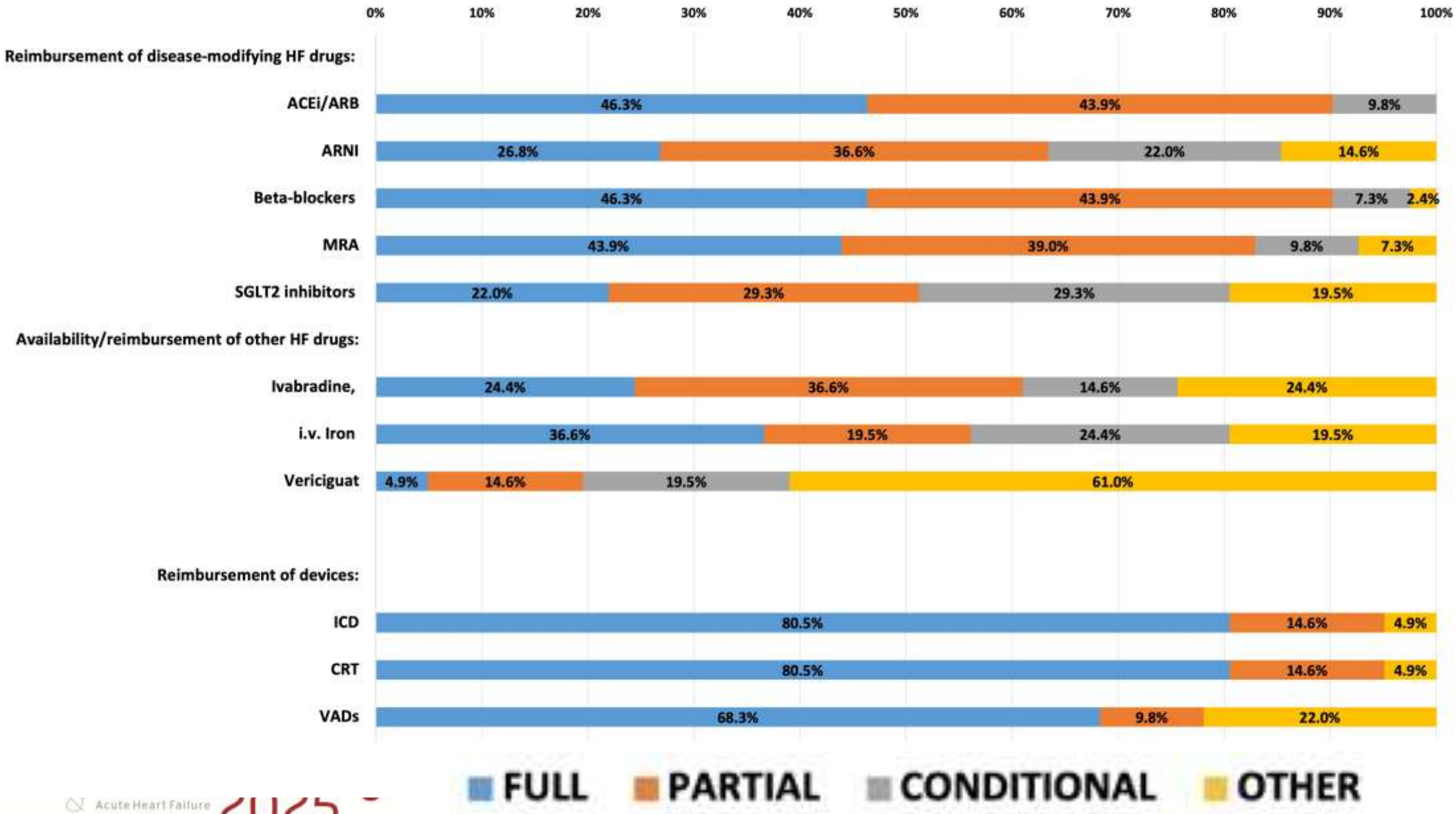


Median No of HF centres: 2.6 per million population

Heart Failure & World Congress on Acute Heart Failure 2025

Seferović P, Polovina M, Savarese G, et al. Eur J Heart Fail. 2025

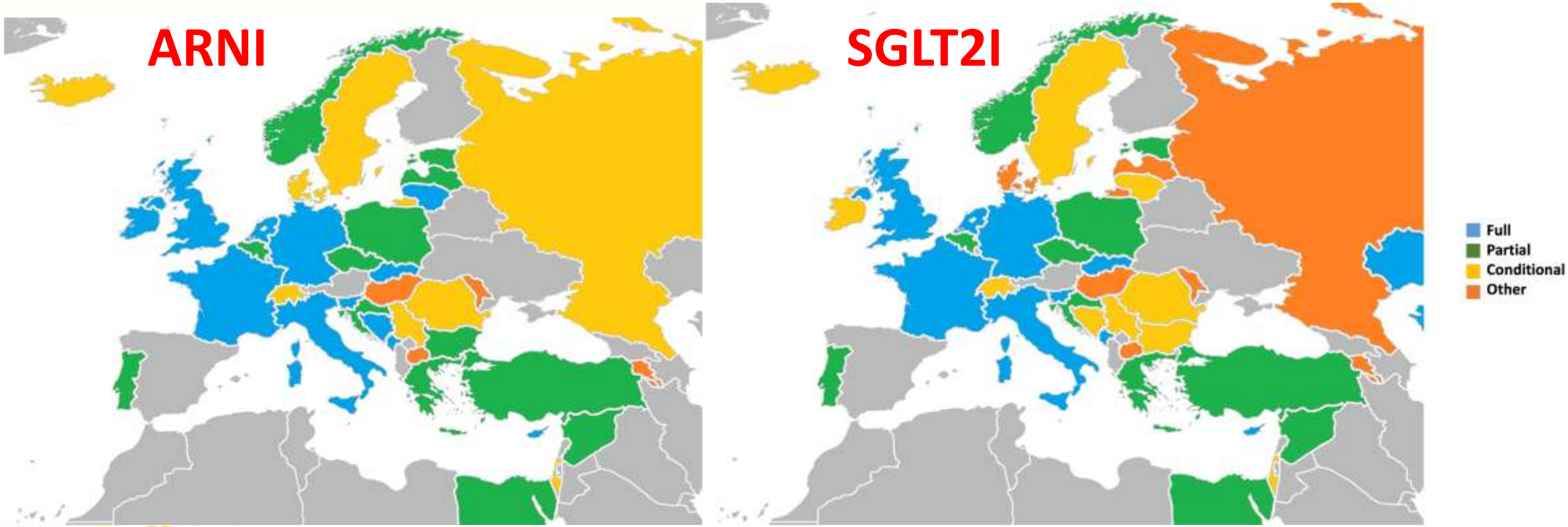
GDMT and device-therapy reimbursement



GDMT and device-therapy reimbursement

European Heart Failure Survey

Public reimbursement of ‘novel’ HF medications is significantly driven by socioeconomic disparities



European Heart Journal

Volume 43, Issue 1
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Article Contents

doi:10.1093/eurheartj/ehab734

Global Spotlights

ESC/HFA Quality of Care Centres: the ultimate frontier in unifying heart failure management

Petar M. Seferovic [1,2]*, Massimo Piepoli [3], Marija Polovina[2,4], Ivan Milinkovic[2,4], Giuseppe M. C. Rosano [5], and Andrew J. S. Coats[6]

[1]Serbian Academy of Sciences and Arts, Belgrade 11000, Serbia; [2]Faculty of Medicine, Belgrade University, Belgrade 11000, Serbia; [3]Heart Failure Unit, Cardiology, G. da Saliceto Hospital, Piacenza I-29121, Italy; [4]Department of Cardiology, University Clinical Center of Serbia, Belgrade 11000, Serbia; [5]Department of Medical Sciences, IRCCS San Raffaele, Rome 00163, Italy; and [6]Faculty of Medicine, University of Warwick, Coventry CV4 7HL, UK

Heart failure (HF) is a major public health concern and a leading global cause of mortality, hospitalization, disability, and high associated healthcare costs. According to the recent Heart Failure Association of the ESC (HFA) Atlas survey of the 42 European Society of Cardiology (ESC) member countries, with a population of ~800 million people, the burden of HF in this region is estimated to involve ~14 million patients, ~2.5 million hospitalisations, and ~2.4 million new cases annually.[1] Multidisciplinary management of HF, defined as patient-centred, multi-specialist and coordinated care from primary to tertiary levels, has been shown to effectively improve outcomes and optimize the utilization of resources.[2] However, the HFA Atlas has demonstrated that there are significant disparities in healthcare organization and available resources for its management across Europe that result in the heterogenous delivery of contemporary diagnostic modalities and guideline directed therapies (GDT).[1] Furthermore, in most countries, dedicated institutions for HF management (i.e. HF centres) are sparse and insufficient to accommodate for the growing demands for expert HF care.[1]

12 Central Eastern Europe countries

21 participating centres

N=2251 pts

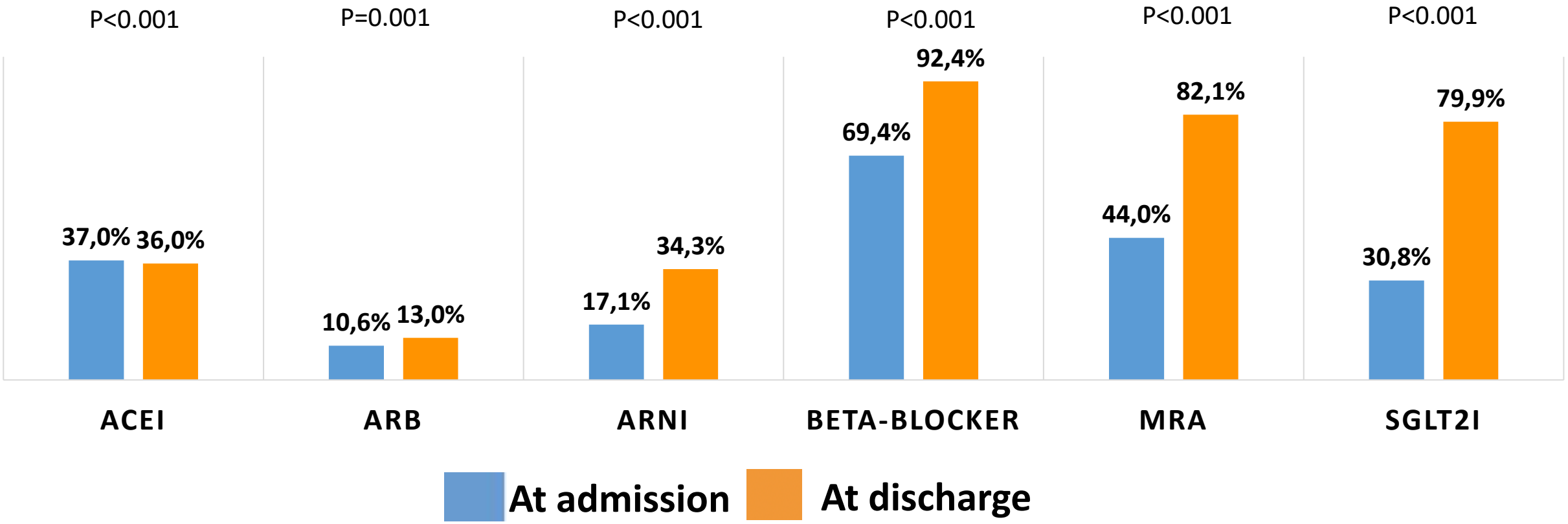
Multinational, multicentre,

investigator-initiated survey with following goals:

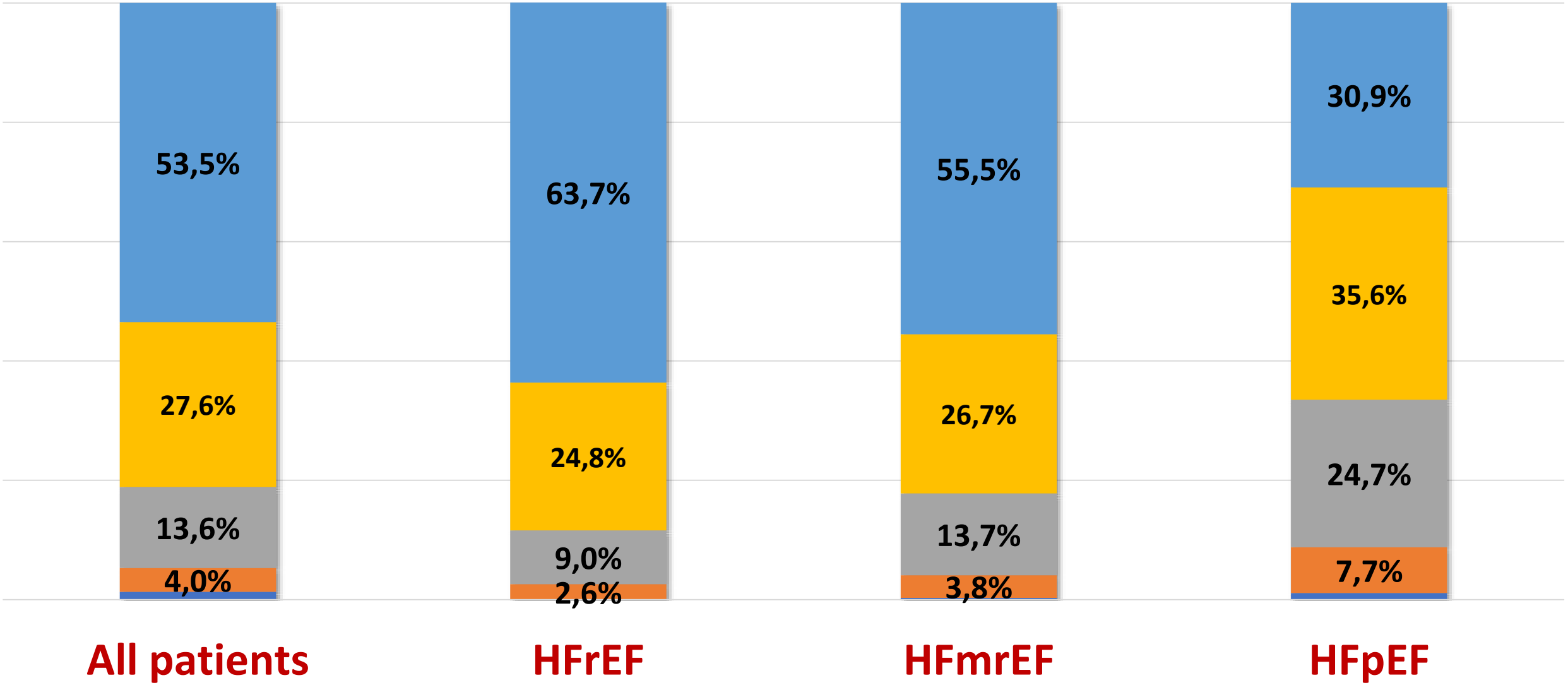
1. Information on clinical and demographic characteristics and HF clinical phenotypes;
2. To assess pre- and post-discharge adherence to the 2021 GL;
3. To identify the reasons for GDMT underutilization or underdosing;
4. To evaluate the use of ICD and CRT-D or CRT-P in patients with HFrEF

2. Admission and predischarge GDMT: all patients n=2251

All patient regardless of LVEF



Total number of HF medication classes at discharge



3. Determinants of GDMT predischarge underutilisation: all patients, n=2251

Multivaribale logistic regression analysis for the provision of <three GDMT classes

Variable	OR	95% CI	P-value
Age (years)	1,02	1,01 - 1,03	0,002
Education (primary)	1,47	1,06 - 2,03	0,020
Living alone	1,54	1,13 - 2,11	0,007
Duration of hospital stay (days)	1,04	1,02 - 1,06	0,007
Nonischaemic HF aetiology	1,45	1,07 – 1,96	0,015
LVEF (%)	1,04	1,03 - 1,05	<0,001
Hypotension (SBP predischarge <100 mmHg)	2,94	1,82 - 4,75	<0,001
Hyperkalaemia (predischarge K+ >5.5)	2,43	1,43 - 4,12	0,001
CKD	1,75	1,32 - 2,32	<0,001
Predischarge edema	1,73	1,29 - 2,32	<0,001

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.70031

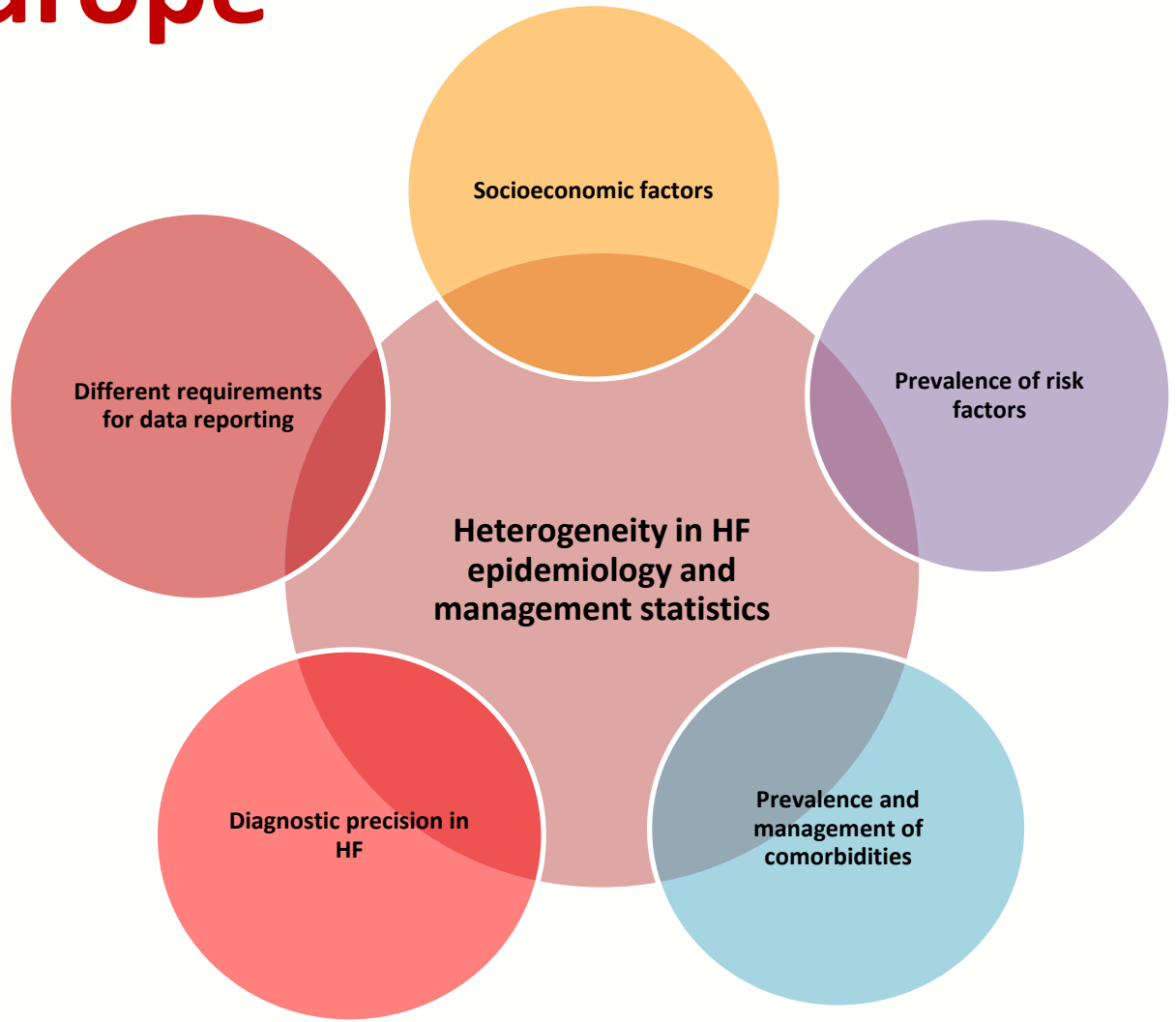
RESEARCH ARTICLE

Contemporary implementation of guideline-directed medical and device therapies in heart failure: Insights from the Central/Eastern Europe Quality of Care Centres Survey

Petar M. Seferović[1,2*], Marija Polovina[1,3], Jan Krejči[4], Bela Merkely[5], Mariya Tokmakova[6], Martin Huelssmann[7], Vladimir Miloradović[8,9], Svetlana Apostolović[10,11], Elizabeta Srbinovska-Kostovska[12], Slavica Radovanović[13], Anastazija Stojšić-Milosavljević[14,15], Aleksandra Milovančev[14,15], Marija Zdravković[1,16], Duška Glavaš[17], Tamara Preradović-Kovačević[18,19], Eva Goncalvesova[20], Michal Laufer-Perl[21], Nataša Marković-Nikolić[1,22], Zumreta Kušljugić[23,24], Larisa Hudić-Dizdarević[23,24], Dan Gaita[25], Ginta Kamzola[26], Robert Sepp[27], Dragan Simić[1,3], Arsen Ristić[1,3], Milika Ašanin[1,3], Gordana Krljanac[1,3], Petar Otašević[1,28], Dejana Stanisavljević[1,29], Davor Miličić[30,31], Magdy Abdelhamid[32], and Gianluigi Savarese[33,34], Central/Eastern Europe QCC Survey Young Investigators[†]

The increasing burden of heart failure in Eastern Europe

- Longstanding collaborative effort of the ESC and Eastern Europe Cardiological Societies.
- Up-to-date information.
- Key to understanding HF societal impact and healthcare systems capacities.
- Persistent heterogeneities in HF data highlight the importance of standardized data collection.



Manuel Jimenez Prieto: Martin Charcot visits a patient, 1897