

Insufficienza cardiaca avanzata: ripensare accesso, decisioni e percorsi clinici

Il ruolo etico e clinico dei cardiologi del territorio nei percorsi di referral

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The challenge: achieving the optimal balance



**Prevalence of at least 1
million patients**

The challenge: achieving the optimal balance

How can we achieve the optimal balance between the two competing objectives?

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Identifying and overcoming barriers to referral in advanced heart failure. A scientific statement of the Heart Failure Association (HFA) of the ESC

Guillaume Baudry^{1,2,3,*}, Maria Generosa Crespo-Leiro^{4,5,6}, Clément Delmas^{3,7}, Federica Guidetti^{8,9}, Marta Jimenez-Blanco Bravo¹⁰, Federica Valente¹¹, Maja Cikes¹², Nicolas Girerd¹, Finn Gustafsson¹³, Gianluigi Savarese⁸, Linda W. van Laake¹⁴, Loreena Hill¹⁵, Anne Kathrine Skibelund¹⁶, Andreas Zuckermann¹⁷, Marco Metra¹⁸, and Kevin Damman^{19*}

Preg.

The issue: inadequate knowledge and use

Systematic screening: **INEED HELP** acronym

- **I** - Need for Inotropes.
- **N** - NYHA Class II/IV or persistently high Natriuretic peptides.
- **E** - Worsening End-organ dysfunction (liver, kidney).
- **E** - Ejection fraction < 20%

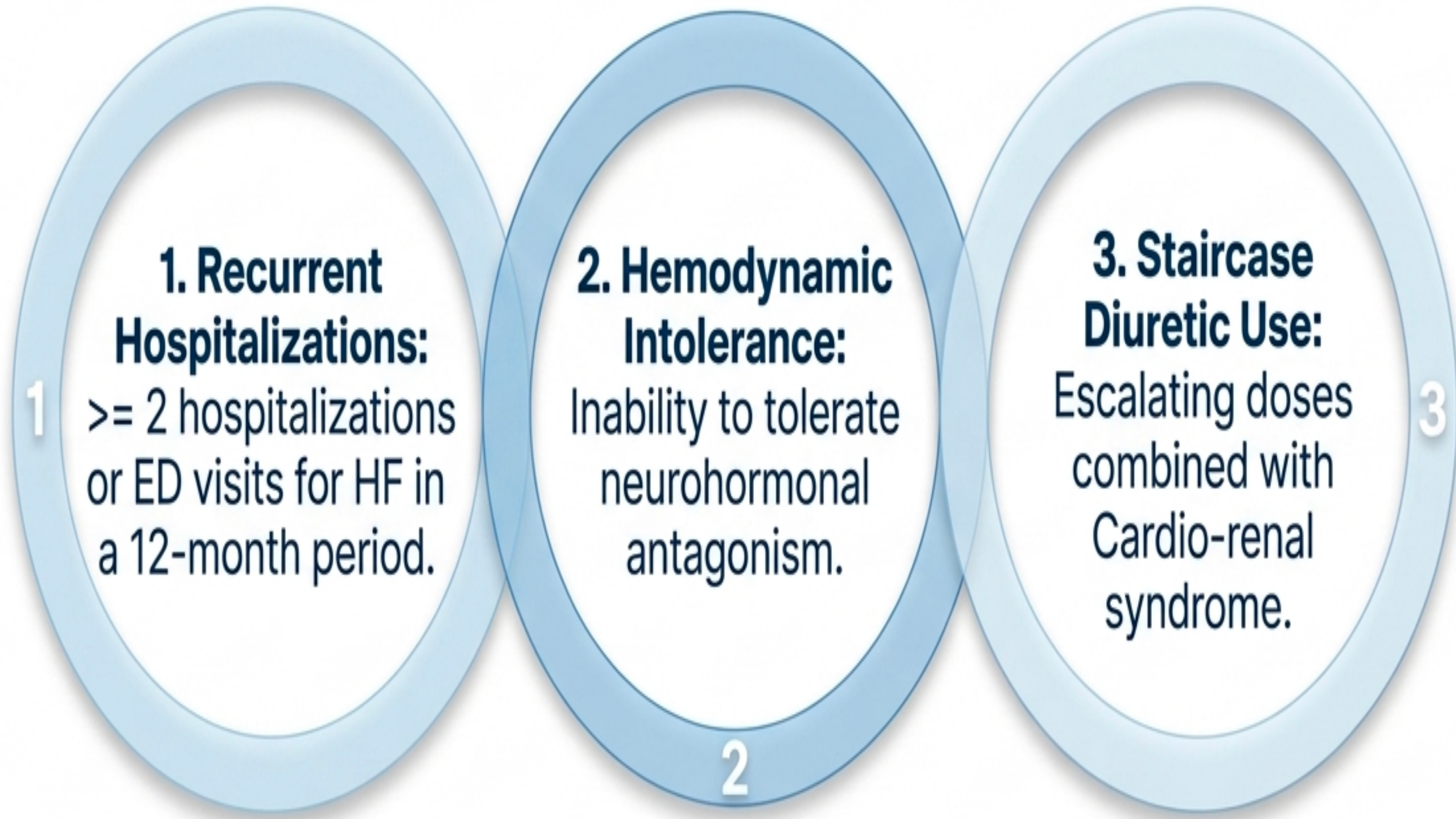
- **D** - Defibrillator shocks for ventricular arrhythmias.
- **H** - >1 Hospitalization for HF in the last year.
- **E** - Edema/ escalating diuretic dose.
- **L** - Low blood pressure (systolic consistently < 90).
- **P** - Prognostic medication intolerance (can't titrate GDMT).

ACTION PATHWAY:

**Any single trigger on this board flags the patient for an immediate
Advanced HF consultation.**

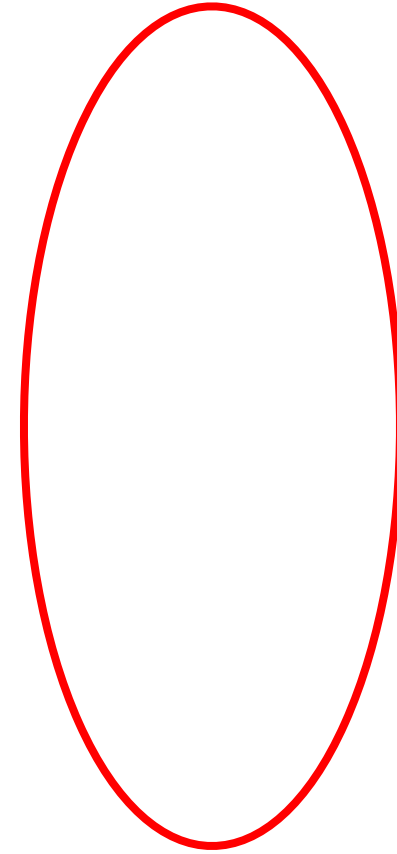
Systematic screening

The rule of three



Systematic screening

The rule of three



**RED FLAG: ≥ 2 hospitalizations in 12 months is a critical clinical indicator correlating to a 1-year mortality rate exceeding 40%.
The patient is no longer stabilizing; they are spiraling.**

Systematic screening

The rule of three

- **Hemodynamic Intolerance:** Systolic Blood Pressure (SBP) consistently < 90 mmHg.
- **GDMT Retreat:** Forced down-titration or discontinuation of ACEi/ARB/ARNI or Beta-blockers due to hypotension or renal shock.
- **Escalating Diuretics:** Daily Furosemide requirement > 160 mg (or equivalent) to maintain euvolemia, signaling severe diuretic resistance.

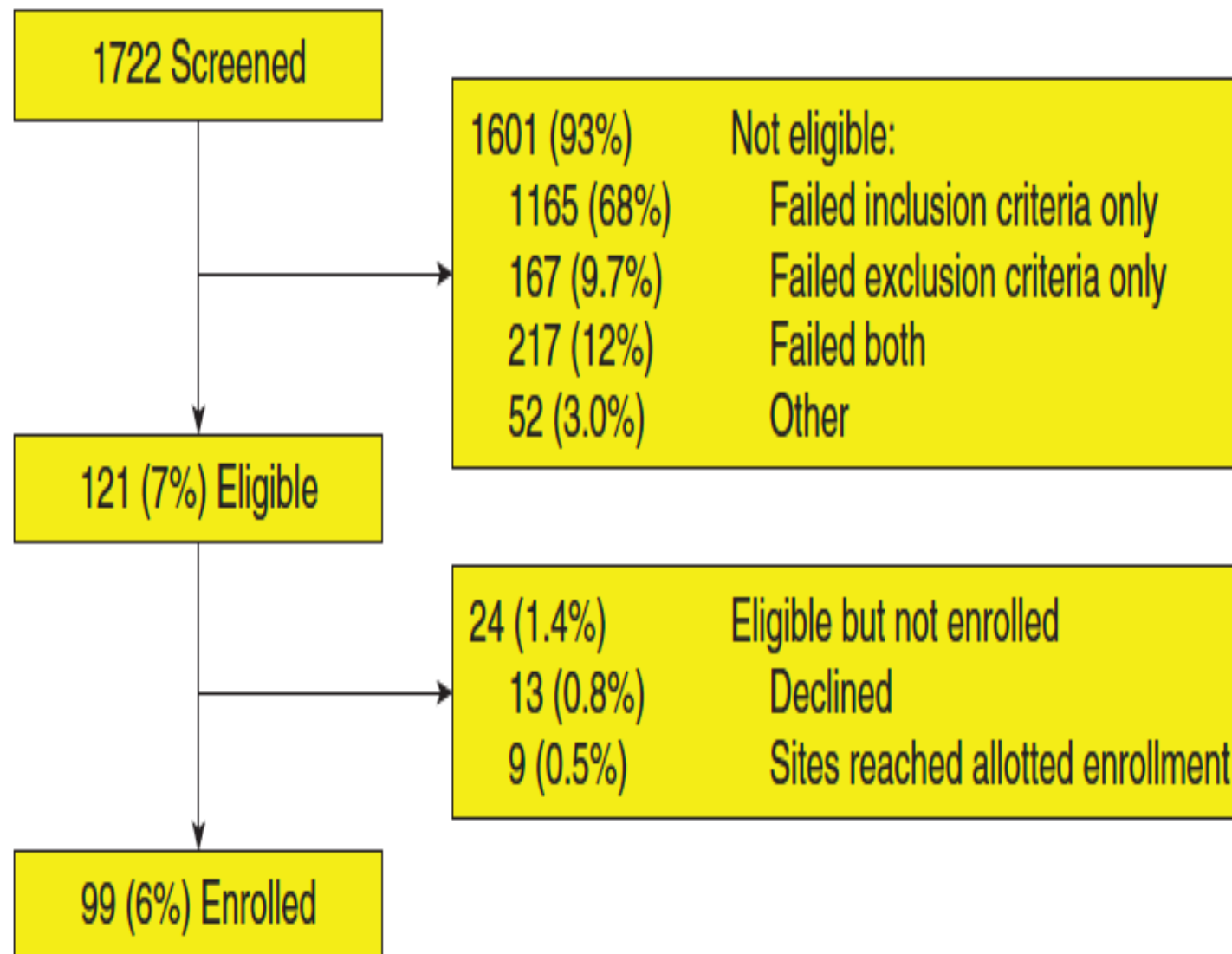
ACTION PATHWAY: When the neurohormonal axis is exhausted, attempts to optimize conventional therapy only increase risk. Pivot immediately to Advanced HF evaluation.

Systematic screening

Role of ecocardiography and natriuretic peptides

Natriuretic Peptides	Threshold: NT-proBNP > 5000 pg/ml persistently, despite euvolemia.
Sodium	Threshold: Persistent Hyponatremia, signaling severe neurohormonal activation and fluid overload.
Echocardiography	Threshold: Marked LV Dilatation with an LVEDD >80mm, indicating irreversible spherical remodeling. - LVEF ≤ 25% paired with pseudonormal or restrictive mitral inflow patterns, indicating stiff, non-compliant ventricles. - Secondary Pulmonary Hypertension

ACTION PATHWAY: These figures eliminate subjectivity; once these thresholds are met, heart failure progresses to an advanced stage, and patients should be referred appropriately.

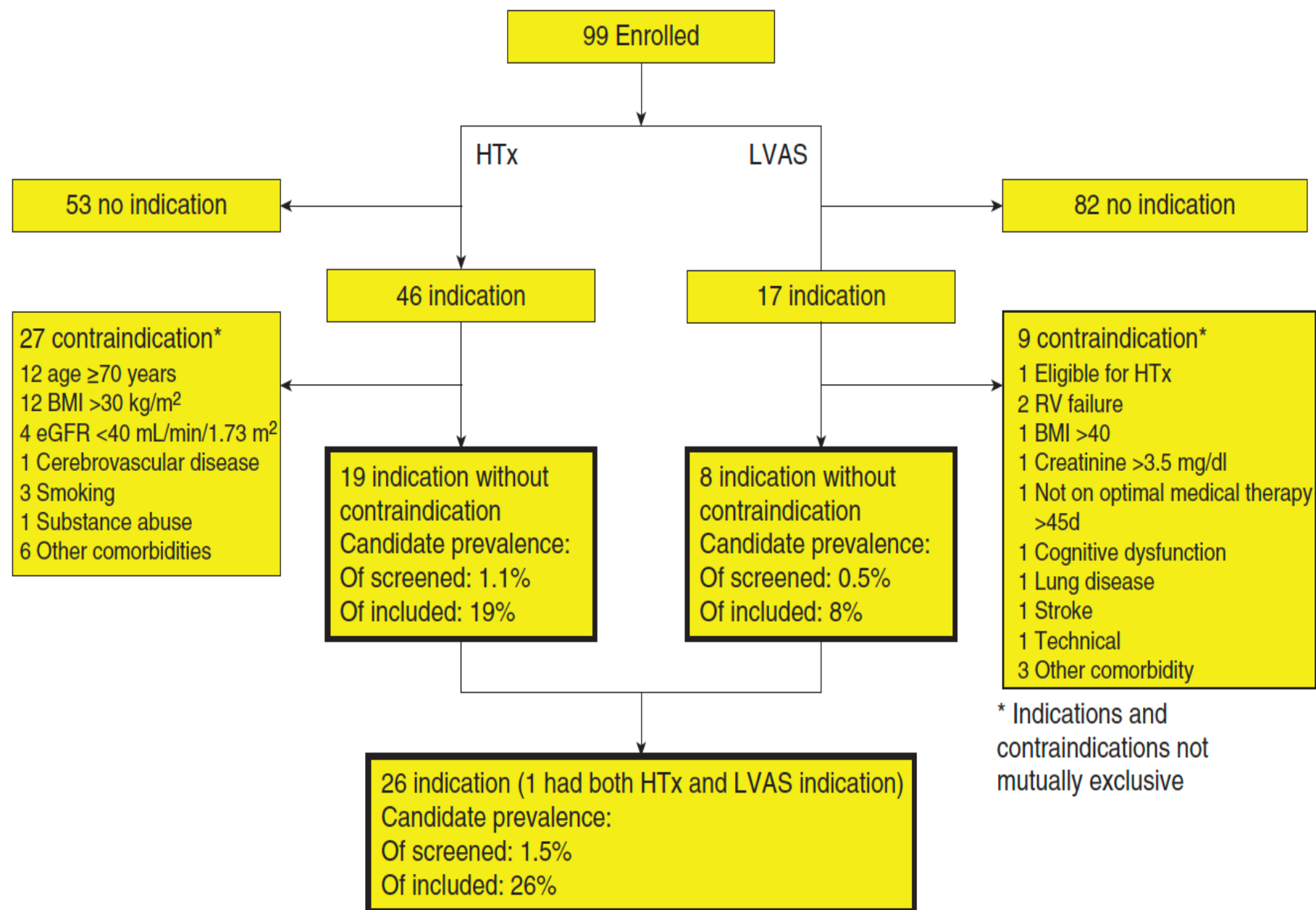


Screening for heart transplantation and left ventricular assist system: results from the ScrEEning for advanced Heart Failure treatment (SEE-HF) study

Lars H. Lund^{1,2*†}, Jean-Noel Trochu^{3†}, Bart Meyns⁴, Kadir Caliskan⁵, Steven Shaw⁶, Jan D. Schmitto⁷, David Schibilsky⁸, Laura Damme^{9†}, Jerry Heatley⁹, and Finn Gustafsson^{10†}

•Inclusion criteria

- 1. CRT and/or ICD device in place.
- 2. NYHA Class III – IV heart failure.
- 3. LVEF < 40%
- 4. Patient is an out-patient.
- 5. Patient is on optimal medical management as tolerated and as defined by the primary care physician.



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Ambulatory Stage C2D Heart Failure Definitions and Current Therapeutic Approaches



JACC: Heart Failure Position Statement

Shannon M. Dunlay, MD, MS,^a Monica Colvin, MD, MS,^b Jennifer A. Cowger, MD, MS,^c Marisa G. Crespo Leiro, MD, PhD,^d Akshay S. Desai, MD, MPH,^e Stephen J. Greene, MD,^f Finn Gustafsson, MD, PhD,^g Shelley Hall, MD,^h Onyedika J. Ilonze, MD, MPH,ⁱ Anuradha Lala, MD,^j Carolyn S.P. Lam, MBBS, PhD, MS,^k Robert L. Page, PHARM.D, MSPH,^l Lars H. Lund, MD, PhD,^m Teresa A. McDonagh, MD,ⁿ Colleen K. McIlvennan, PhD, DNP, ANP,^o Sean P. Pinney, MD,^j Lauren K. Truby, MD,^p Clyde W. Yancy, MD, MSc,^q Biykem Bozkurt, MD, PhD,^r Lynne W. Stevenson, MD^s

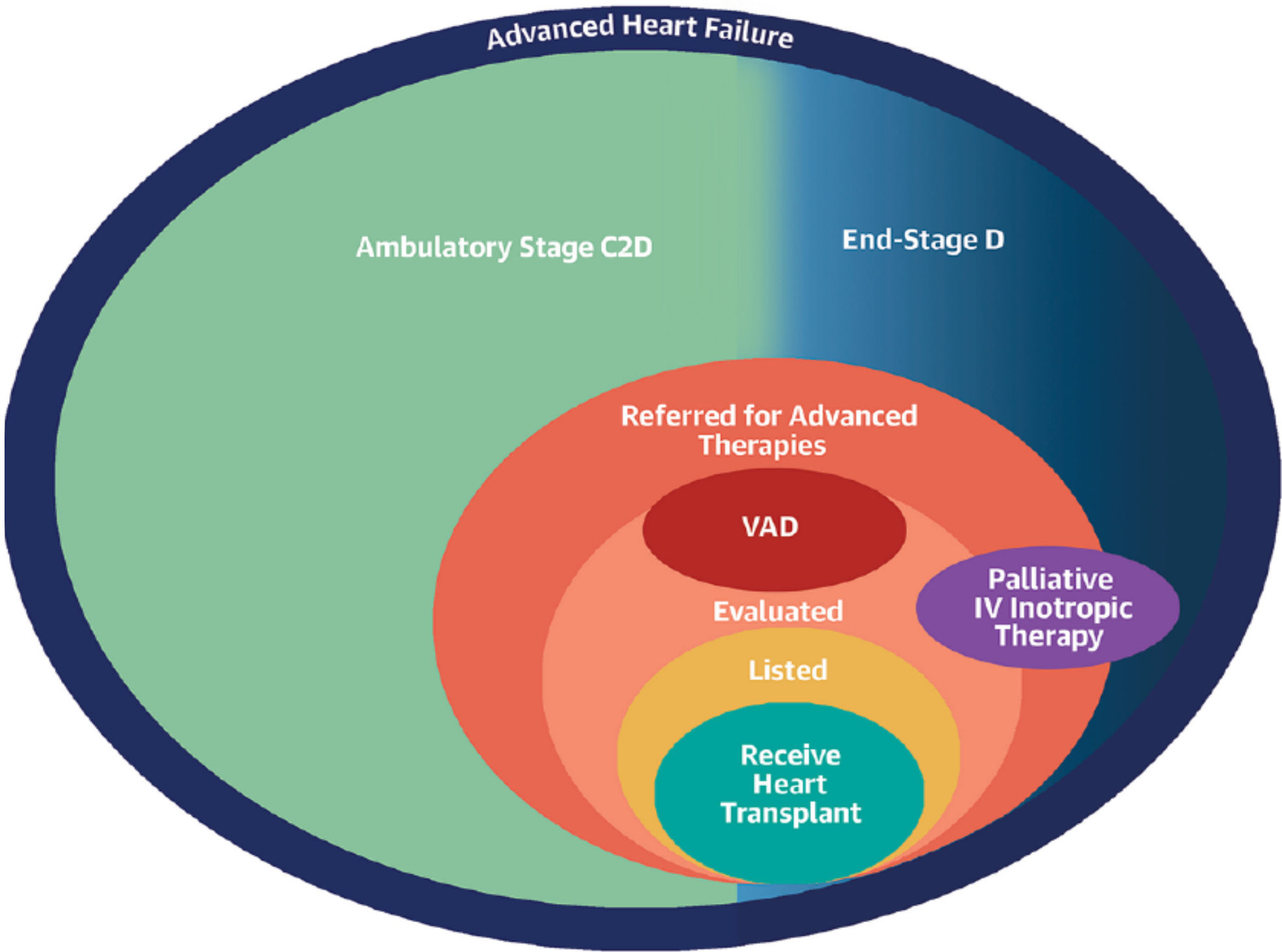
TABLE 1 Proposed Core and Common Features of Stage C2D Heart Failure With Reduced Ejection Fraction

Proposed core features for stage C2D identification (must have all 3):

- Consistent limitation of routine daily life by NYHA functional class III or ambulatory NYHA functional class IV symptoms despite use of stage C GDMT
- Ambulatory life at home without intravenous inotropic support
- Reduced exercise capacity; typically, 6MWD <300-350 m and/or peak Vo₂ 11-15 mL/kg/min

Supportive common features (usually multiple present):

- LVEF typically <25%-30%
- Intolerance or decreasing tolerance for neurohormonal modulation (eg, circulatory-renal limitations to ARNI/ACEI/ARB or beta-blockers)
- Recurrent or persistent clinical congestion requiring diuretic escalation and combination
- Systolic blood pressure frequently <100 mm Hg; may be <90 mm Hg
- Labile and/or declining renal function
- Hospitalizations common; may include intensive care and temporary intravenous inotropes
- Recurrent ventricular arrhythmias
- Worsening mitral and/or tricuspid valvular regurgitation
- High natriuretic peptide levels
- Hyponatremia that is not medication-induced
- Quality of life limited primarily by HF with KCCQ Clinical Summary Score of 45 to 65



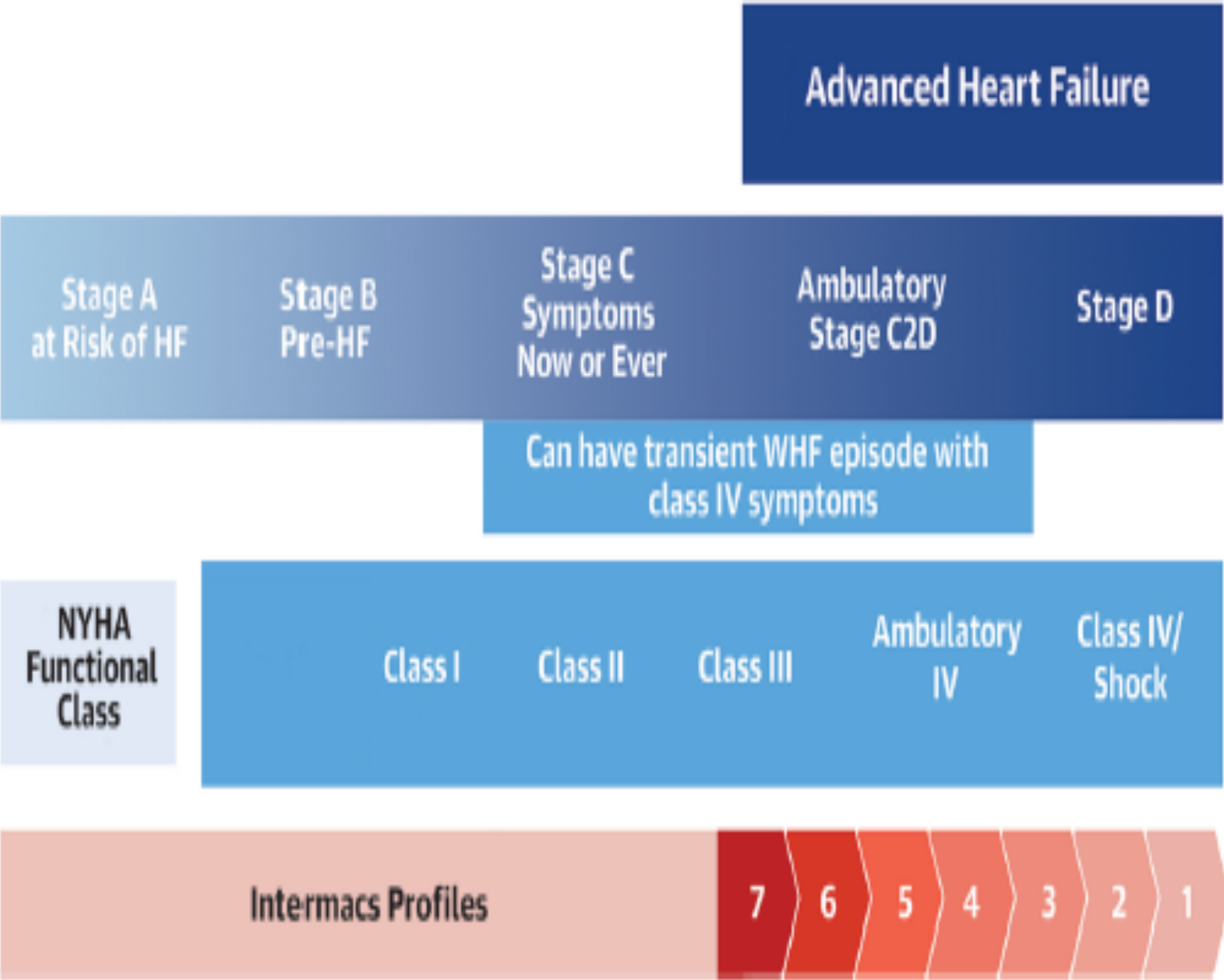
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Advanced HF includes not only end-stage D patients but also a large ambulatory population progressing beyond sustained response to GDMT who still seek and may find meaningful life-years ahead



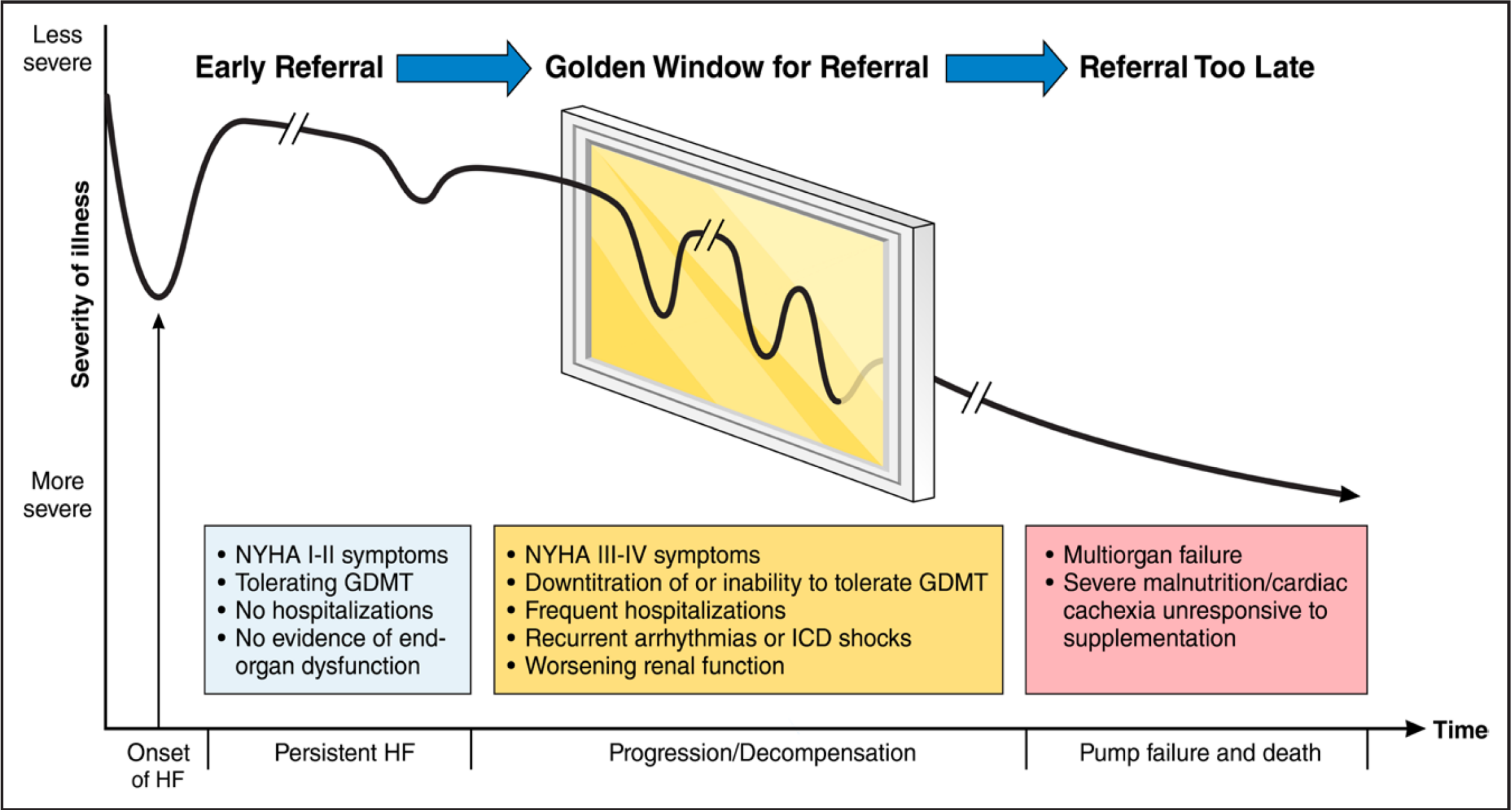
AHA SCIENTIFIC STATEMENT

Guidance for Timely and Appropriate Referral of Patients With Advanced Heart Failure

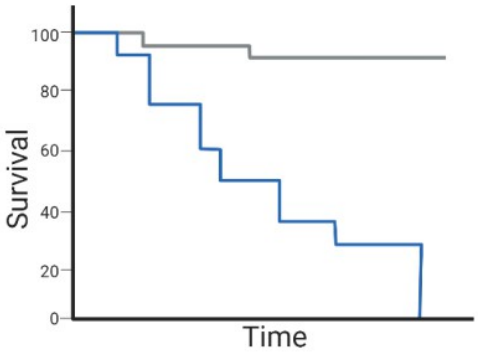
A Scientific Statement From the American Heart Association

Endorsed by the Heart Failure Society of America

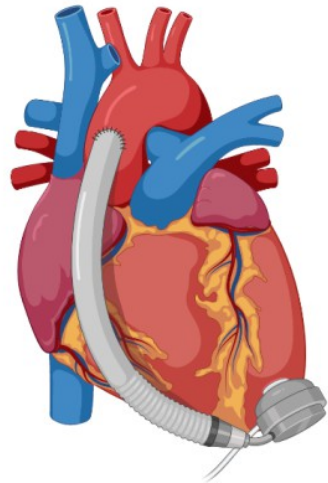
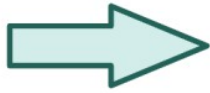
Alanna A. Morris MD, MSc, FAHA, Chair; Prateeti Khazanie, MD, MPH, Vice Chair; Mark H. Drazner, MD, MSc, Vice Chair; Nancy M. Albert, PhD; Khadijah Breathett, MD, MS, FAHA; Lauren B. Cooper, MD, MHS; Howard J. Eisen, MD; Patrick O’Gara, MD; Stuart D. Russell, MD; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; and Council on Hypertension



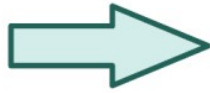
EXPECTED OUTCOMES IN
ADVANCED HF PATIENTS



- Median survival **<1 year** in those dependent on iv inotropic therapy
- Median survival **<2 years** in ambulatory advanced HF not yet on inotropes



LVAD THERAPY



LONG TERM BENEFITS OF LVAD THERAPY

SURVIVAL



Median survival of **5 years**

FUNCTIONAL STATUS

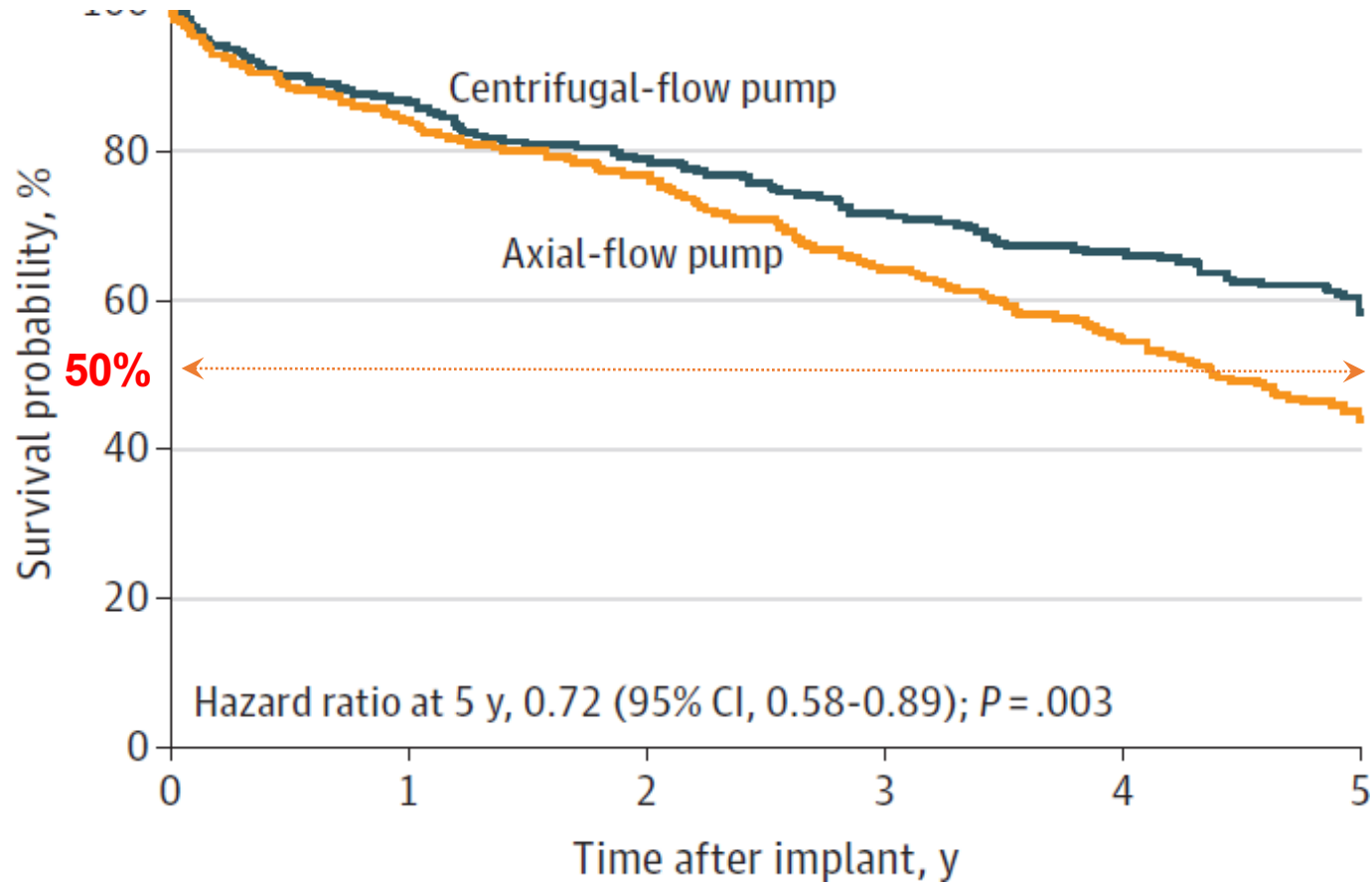


- **NYHA class I-II** in 75-80% at 2 years
- **2.5 fold** improvement in 6MWD (to >300 meters at 2 years)

QUALITY OF LIFE



- **>75% increase** in KCCQ score (+30 points)



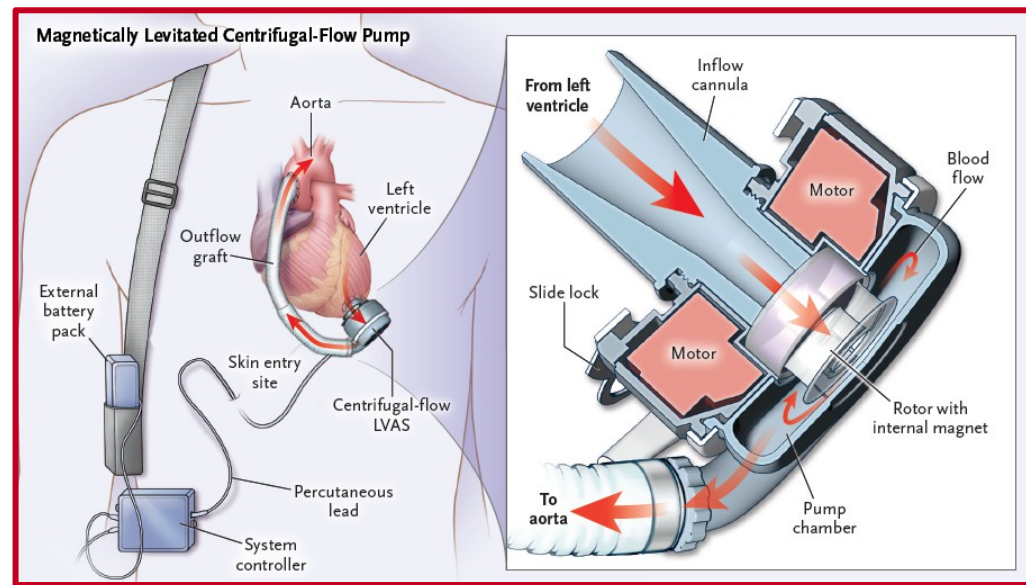
Mehra, Naka, Uriel et al *N Engl J Med.* 2017;376(5):440-450

Adverse Events

Cause of death	Difference, % (95% CI) % ^a	Hazard ratio (95% CI)	Favors centrifugal-flow pump	Favors axial-flow pump	<i>P</i> value ^b
Hemocompatibility-related event (device thrombosis, stroke, bleeding)	-6.8 (-10.0 to -3.6)	0.33 (0.20-0.55)			<.001
Heart failure	0.6 (-2.9 to 4.1)	1.01 (0.67-1.53)			.95
Infection	-0.1 (-2.8 to 2.6)	0.92 (0.54-1.59)			.77
Other ^c	0.0 (-4.1 to 4.0)	0.94 (0.66-1.33)			.72

The median survival exceeds 5-years
with the fully magnetically levitated centrifugal flow
HeartMate 3 LVAD in patients with advanced Heart
Failure

A New Survival and Functional Status Benchmark with Contemporary LVAD Therapy

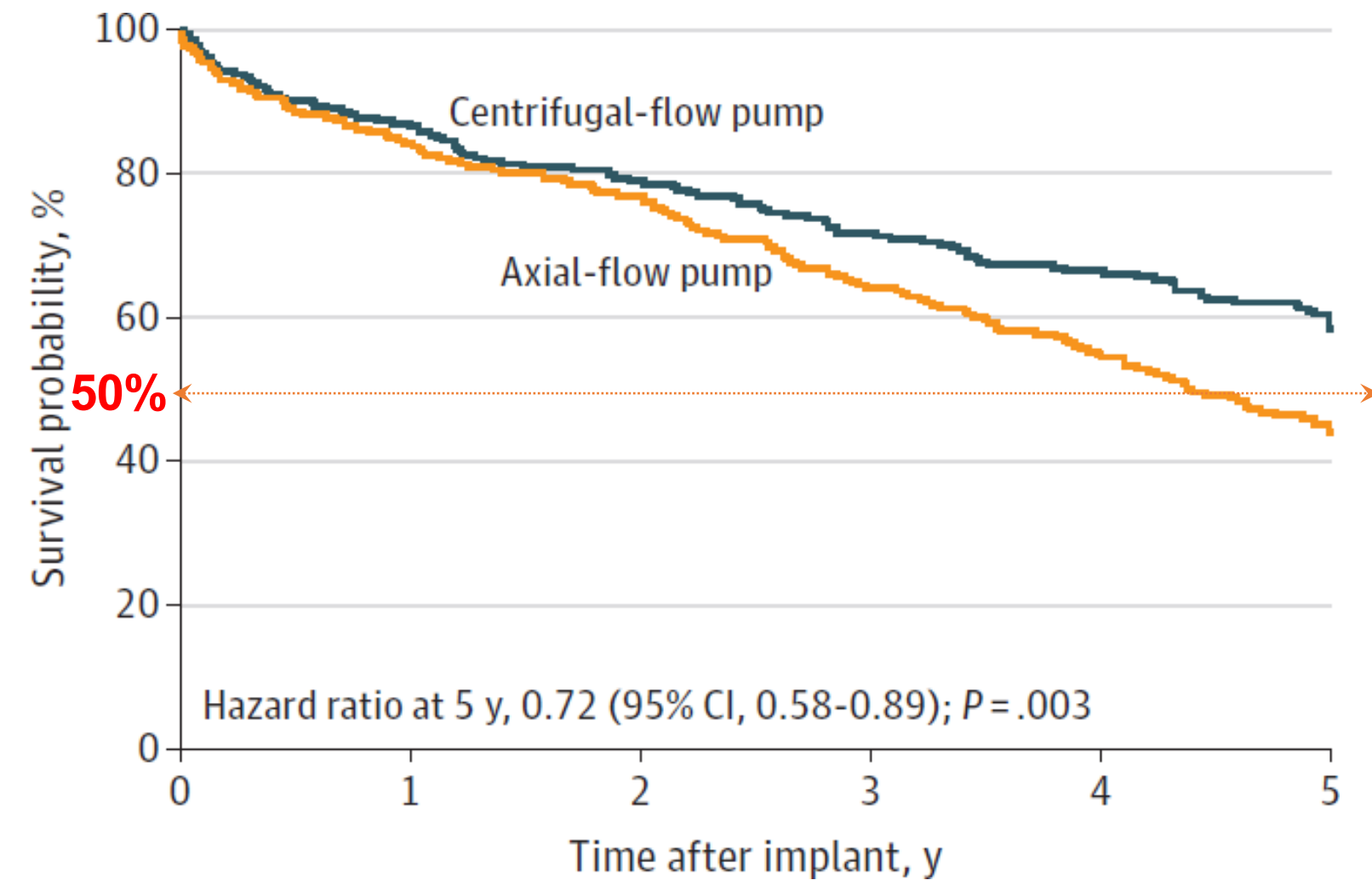


Mehra, Naka, Uriel et al *N Engl J Med*. 2017;376(5):440-450

**FUNCTIONAL
STATUS**



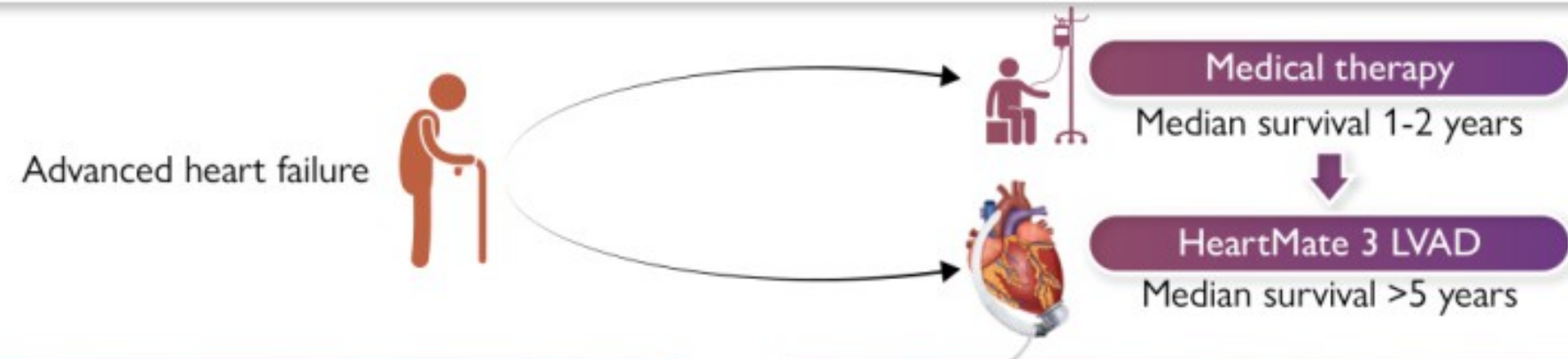
NYHA class I-II in 68%
6 MWD increase of >200 meters



5-year survival of 58.4% on the centrifugal flow HeartMate 3 pump in advanced HF patients irrespective of therapeutic intent

Mehra MR, JAMA. 2022

Evolution of a fully magnetically levitated LVAD in advanced heart failure

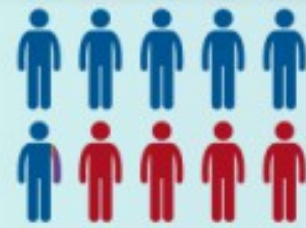


Concordance of Trial and Real-world Evidence

Clinical trial experience

MOMENTUM 3-Randomized Controlled Trial (USA)

Five-year survival



Quality of life EQ-5D VAS*

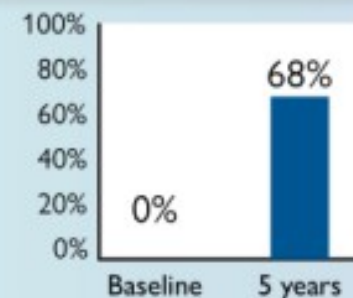


Functional capacity at five years

6MWD



NYHA class I-II



$\frac{2}{3}$ with none to mild symptoms

Real world experience

ELEVATE Registry (Non-USA, Global)

Five-year survival



Quality of life EQ-5D VAS*

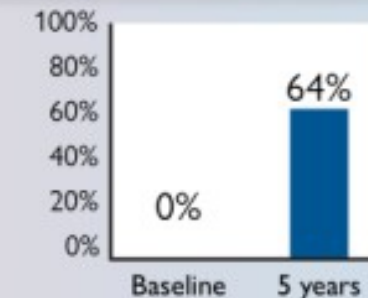


Functional capacity at five years

6MWD



NYHA class I-II



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Key highlights

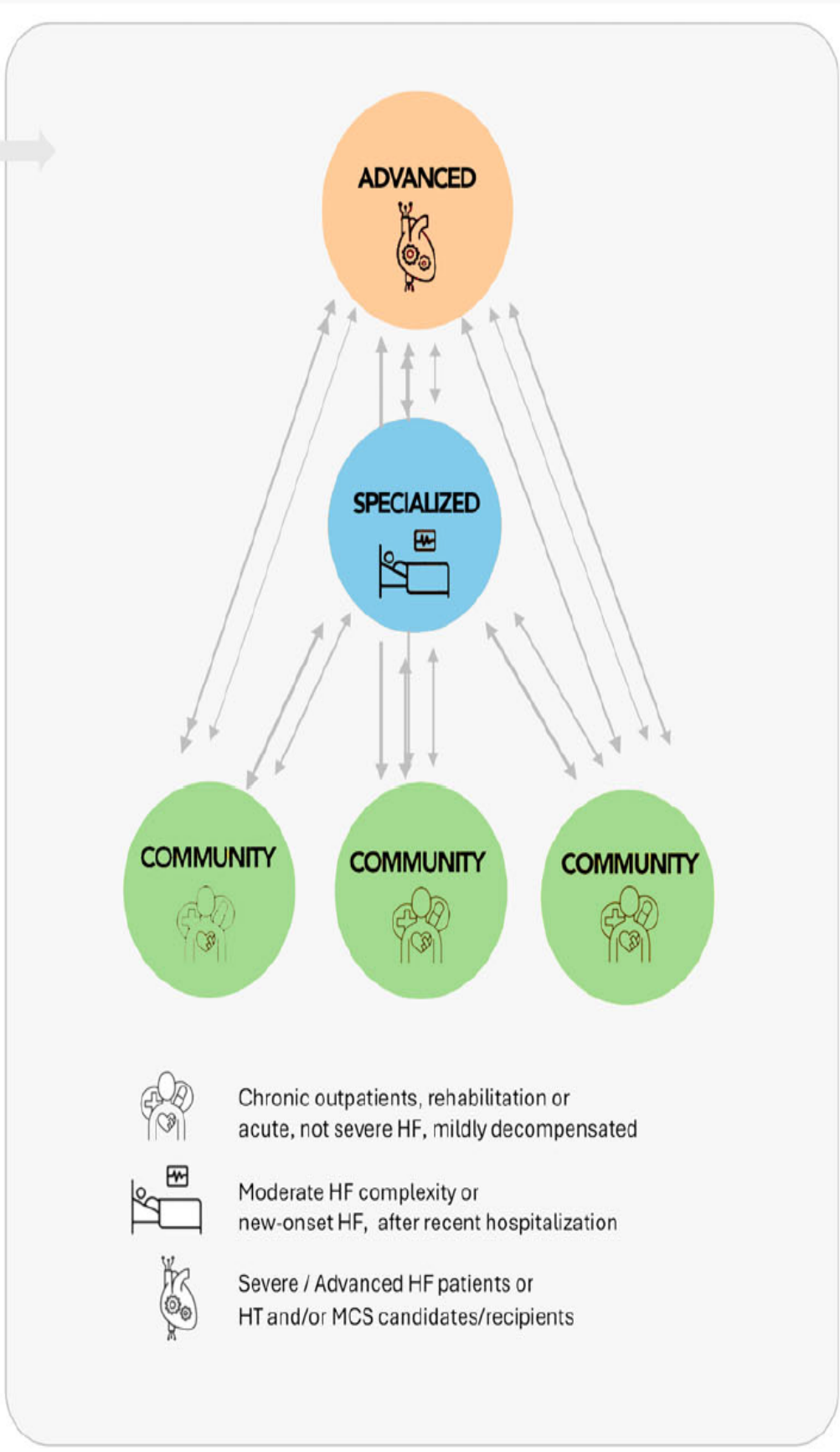
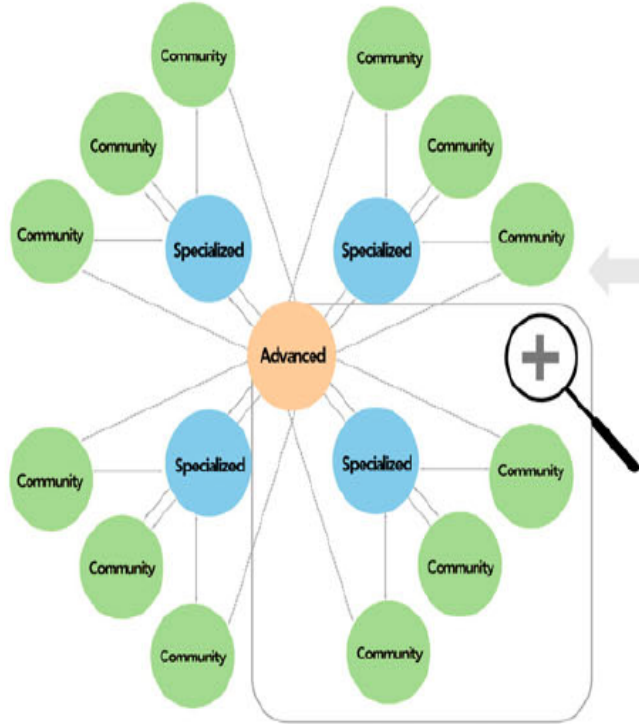
- Despite geographical and healthcare-system heterogeneity, the clinical trial and the real-world experiences demonstrate strikingly similar outcomes
- The burden of device related complications and gains in quality of life and functional capacity show minimal variation across the global experience
- These long-term findings confirm and establish the fully magnetically levitated LVAD as a global therapeutic standard to add years to life and life to years in patients with advanced heart failure irrespective of transplant eligibility

The issue: inadequate network

Preg.

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	COMMUNITY Center	SPECIALIZED HF Center	ADVANCED HF Center
TARGET PATIENTS	Chronic outpatients / rehabilitation Acute, not severe HF / mildly decompensated	Moderate HF complexity, New-onset HF / after recent hospitalization	Severe / Advanced HF patients HT and/or MCS candidates/ recipients
SETTINGS	Primary care Cardiology / rehabilitation Community hospital	CCU / ICU / chest pain unit and specialized wards in district hospitals	As in specialized QCC + Heart Surgery
ACCESSIBILITY	Elective Prompt (<48h) access if needed	On-Duty cardiologist 24/7 CCU/ICU dedicated beds	As in specialized QCC + Cardiac surgery in a heart team + ICU dedicated beds
SERVICE / EQUIPMENT	Therapeutic optimization Patient & caregiver education Rehabilitation ECG, TTE, 24h ECG/BP Holter, laboratory tests Referral to higher level centers	Etiology assessment, Therapeutic optimization, Cardiac catheterization, Arrhythmia ablation, ICD/CRT implantation TOE, CMR, CPET Renal replacement therapy	As in specialized QCC + Circulatory Support Perform HT and/or MCS and/or provide support Cardiac surgery Valve intervention. EMB, genetic testing
HUMAN RESOURCES	Internists /Cardiologists Primary care Nurses	HF Cardiologist 24/7, HF nurses, Other specialties	Advanced HF cardiologist Cardiac surgeons 24/7 Heart team



Grazie