Treatment of the Advanced Heart Failure Patient

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Disclosures

Previous Speaker For Novartis

Speaker for AbioMed

Speaker for BI and Eli-Lilly

Tar Heel Fan

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Definitions

A complex clinical syndrome that occurs when the heart is unable to meet the metabolic demands of the body at normal cardiac filling pressures.

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How Serious Is the Problem?

6.2 million people in the United States with Heart Failure

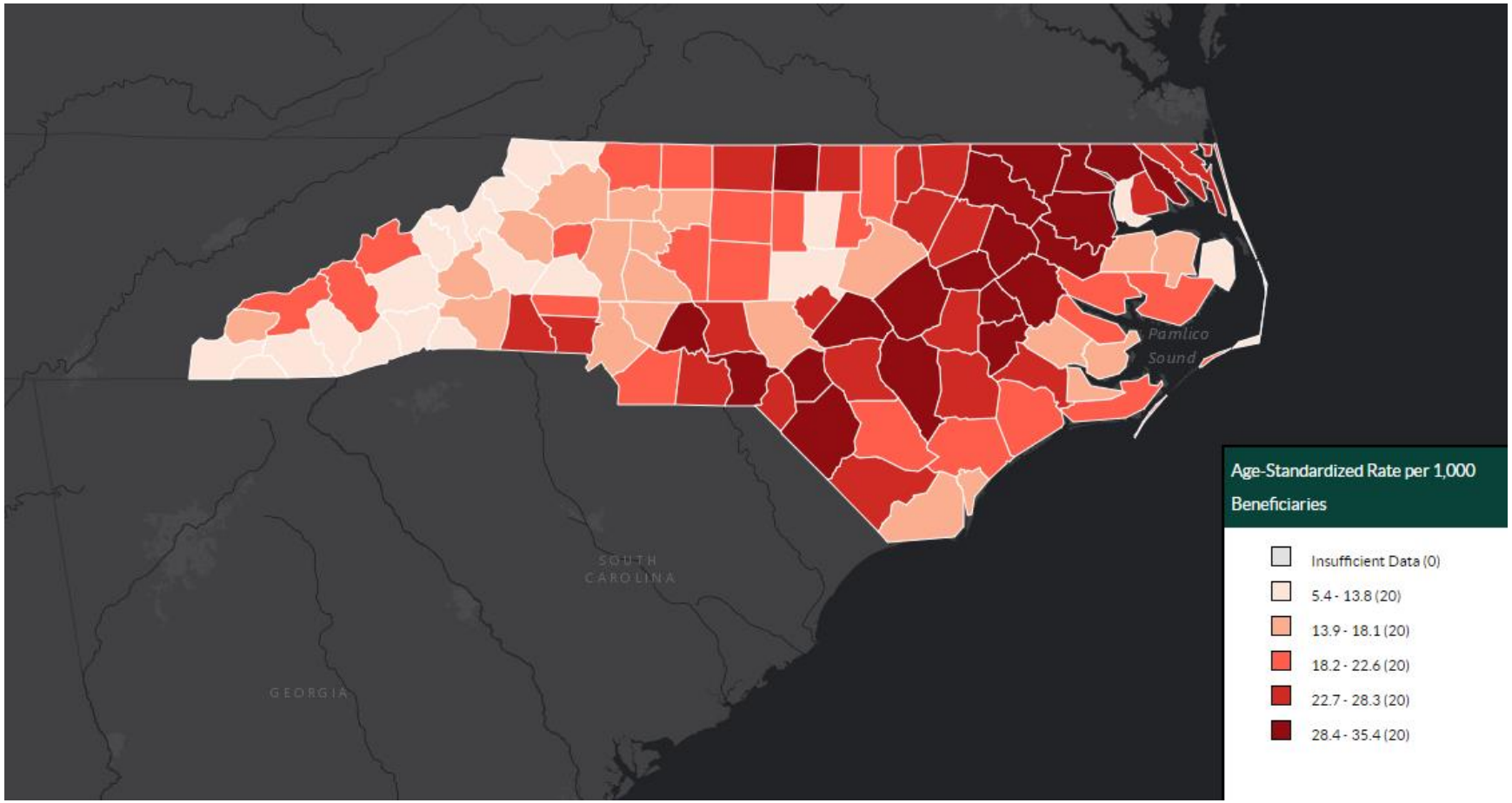
26 million cases worldwide

1/5 people over the age 40 will get diagnosed with heart failure

500,000-650,000 new cases a year

The incidence increases over a person's lifetime

Hospitalizations



CDC interactive Map

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Mortality

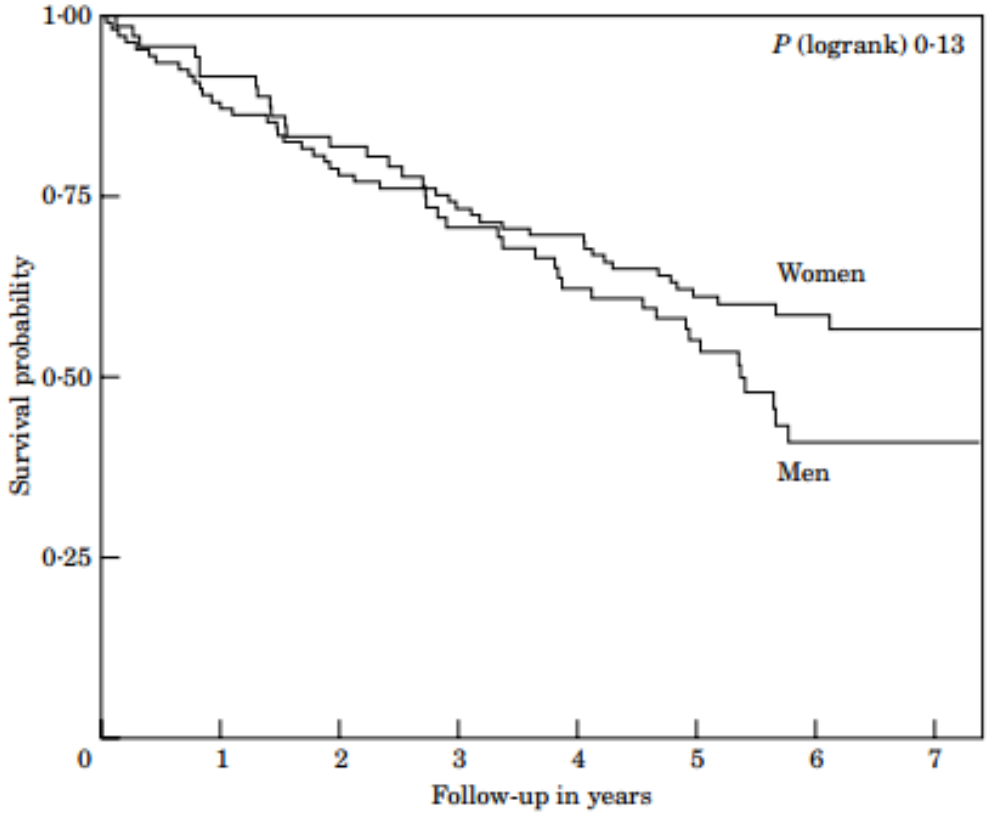

Figure 1 **Kaplan–Meier survival curves for 72 men (74·5 ± 7·4 years) and 109 women (79·2 ± 7·8) with heart failure.**

Mosterd et. Al, European Heart Journal, 2001

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Mortality

Stage D, NYHA Class IV	50% Mortality
Acute cardiogenic shock	Imminent
End organ dysfunction	1 month
Inotrope-dependent	3-6 months
ACE-inhibitor intolerant	6 months
Cachexia, hyponatremia, CKD	6-12 months
Tolerating oral therapies	± 12 months
Stabilized to NYHA Class III	> 24 months

Stevenson LW, Rose EA. Circulation 2003;108:3059

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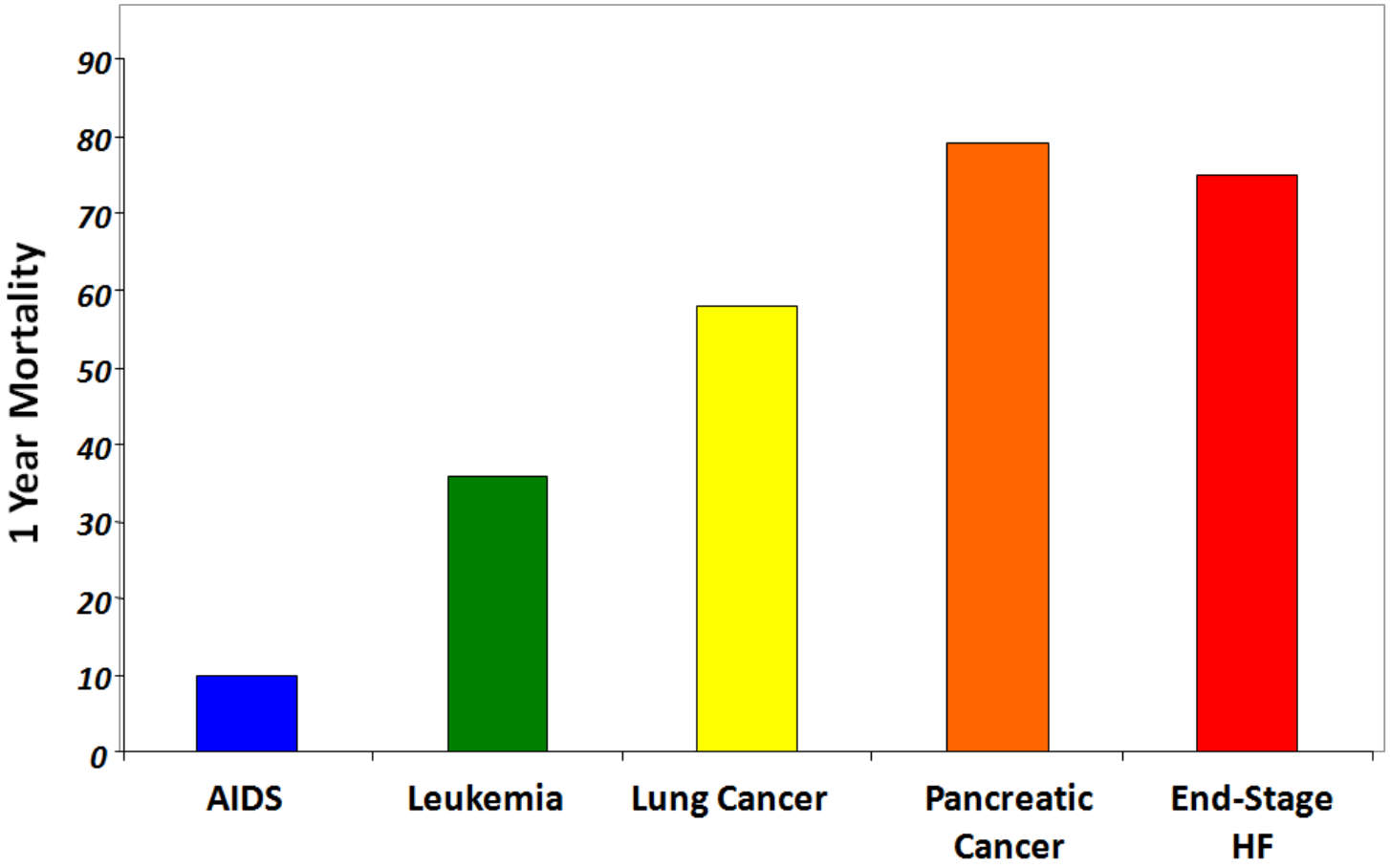
Heart Failure in Context…



Rose EA, et al. Long-term mechanical left ventricular assistance for end-stage heart failure. N Engl J Med. 2001 Nov 15;345(20):1435-43

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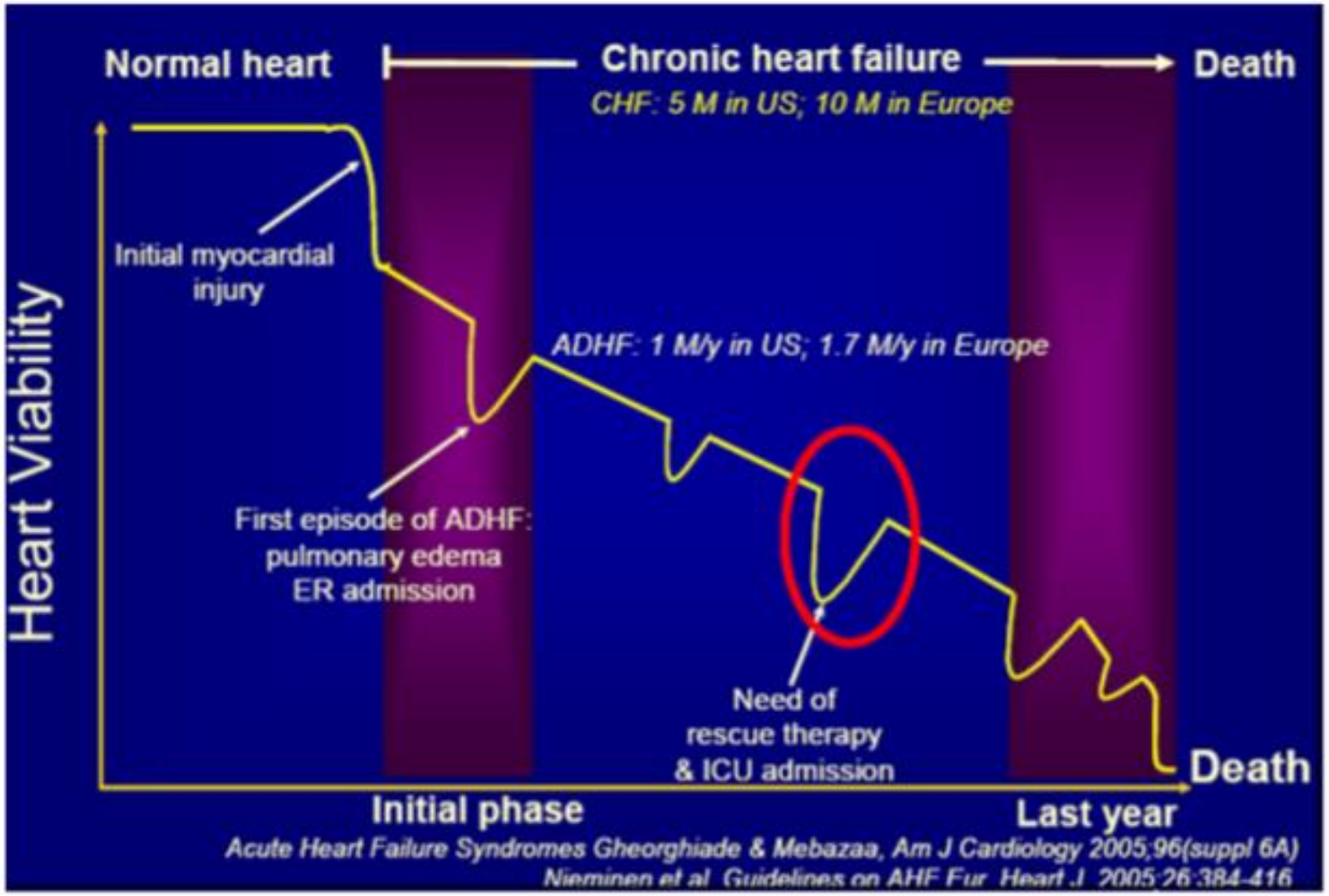
Mortality



Nieminem et. al

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When Patients Reach “End Stage”

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Defining End Stage

NYHA class IIIb-IV despite optimal medical treatment

Intolerant to oral therapies due to hypotension/end organ dysfunction

Volume overload resistant to diuretics

Increasing hospitalizations

Increasing life threatening arrhythmias

High risk scores in a heart failure mortality predictor model

Class 1: No symptoms

Class 2: Mild symptoms with normal activity

Class 3: Moderate symptoms with normal activity

Class 4: Symptoms at rest

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Cardiac Transplant

Only “cure” for heart failure

First case was done 12/3/1967

Major improvements came in 1983 when Cylosporine became available

>100,000 transplants have been done all across the world

Average survival is 10.9 years

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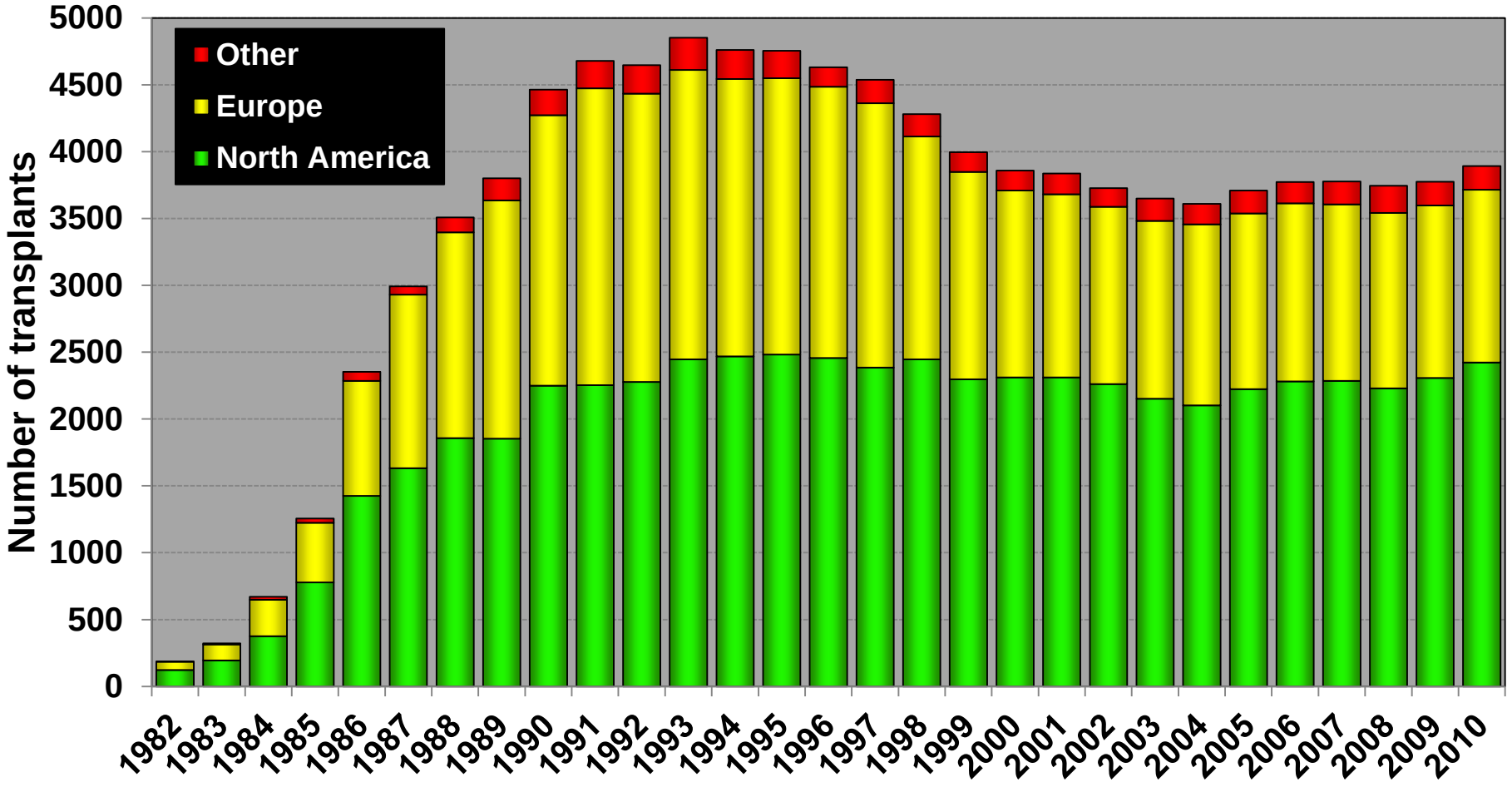
Cardiac Transplant



J Heart Lung Transplant. 2012 Oct; 31(10): 1045-1095

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Cardiac Transplant

Region	UNOS Status at Listing	Year Listed	Registrations Added	Median Waiting Time (Days)	95% Confidence Interval
U.S.	Heart Status 1A	2003-2006	2930	64	(57, 73)
U.S.	Heart Status 1B	2003-2006	3152	79	(74, 86)
U.S.	Heart Status 2	2003-2006	5302	293	(269, 324)
U.S.	Heart Status 1A	2007-2010	3701	67	(61, 73)
U.S.	Heart Status 1B	2007-2010	4453	133	(121, 144)
U.S.	Heart Status 2	2007-2010	4965	465	(432, 506)
U.S.	Heart Status 1A	2011-2014	4659	87	(80, 95)
U.S.	Heart Status 1B	2011-2014	5940	253	(240, 273)
U.S.	Heart Status 2	2011-2014	4457	726	(657, 817)

*Data subject to change based on future data submission or correction. * Denotes a Median Waiting Time was not computed due to N less than 10, or fewer than half the registrants have been transplanted.*

CDC public reported Data.

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Cardiac Transplant

	All Donor Types
To Date	84,297
2022	918
2021	3,817
2020	3,658
2019	3,552
2018	3,408
2017	3,244
2016	3,191
2015	2,804
2014	2,655
2013	2,531
2012	2,378
2011	2,322
2010	2,332
2009	2,212
2008	2,163
2007	2,209
2006	2,193
2005	2,125
2004	2,015
2003	2,057
2002	2,155
2001	2,202

CDC public reported Data.

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Cardiac Transplant

Status	Clinical Criteria
1a	MCS with device-related complication Continuous mechanical ventilation Continuous infusion of multiple inotropic agents or a single agent at high-dose
1b	VAD implanted Continuous inotrope usage
2	Does not meet criteria for 1a/1b
7	Temporarily paused

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Cardiac Transplant

1	VA-ECMO	✓
	Non-dischargeable, surgically implanted, non-endovascular biventricular support device	✓
	MCSD with life threatening ventricular arrhythmia	✓
2	Non-dischargeable, surgically implanted, non-endovascular LVAD	✓
	TAH, BiVAD, RVAD, or VAD for single ventricle patients	
	MCSD with malfunction	✓
	Percutaneous endovascular MCSD	✓
	IABP	✓
	VT or VF	✓
3	Dischargeable LVAD for discretionary 30 days	
	Multiple inotropes or a single high-dose inotrope and hemodynamic monitoring	✓
	MCSD with hemolysis	
	MCSD with pump thrombosis	
	MCSD with right heart failure	
	MCSD with device infection	
	MCSD with mucosal bleeding	✓
	MCSD with AI	
	VA-ECMO after 7 days	✓
	Non-dischargeable, surgically implanted, non-endovascular LVAD after 14 days	✓
	Percutaneous endovascular circulatory support device after 14 days	✓
	IABP after 14 days	✓
4	Dischargeable LVAD without discretionary 30 days	
	Inotropes without hemodynamic monitoring	
	Congenital heart disease	
	Ischemic heart disease with intractable angina	
	Amyloidosis, or hypertrophic or restrictive cardiomyopathy	
	Heart re-transplant	
5	On the waitlist for at least one other organ at the same hospital	
6	Adult candidate suitable for transplant	
7	Patient is inactive	

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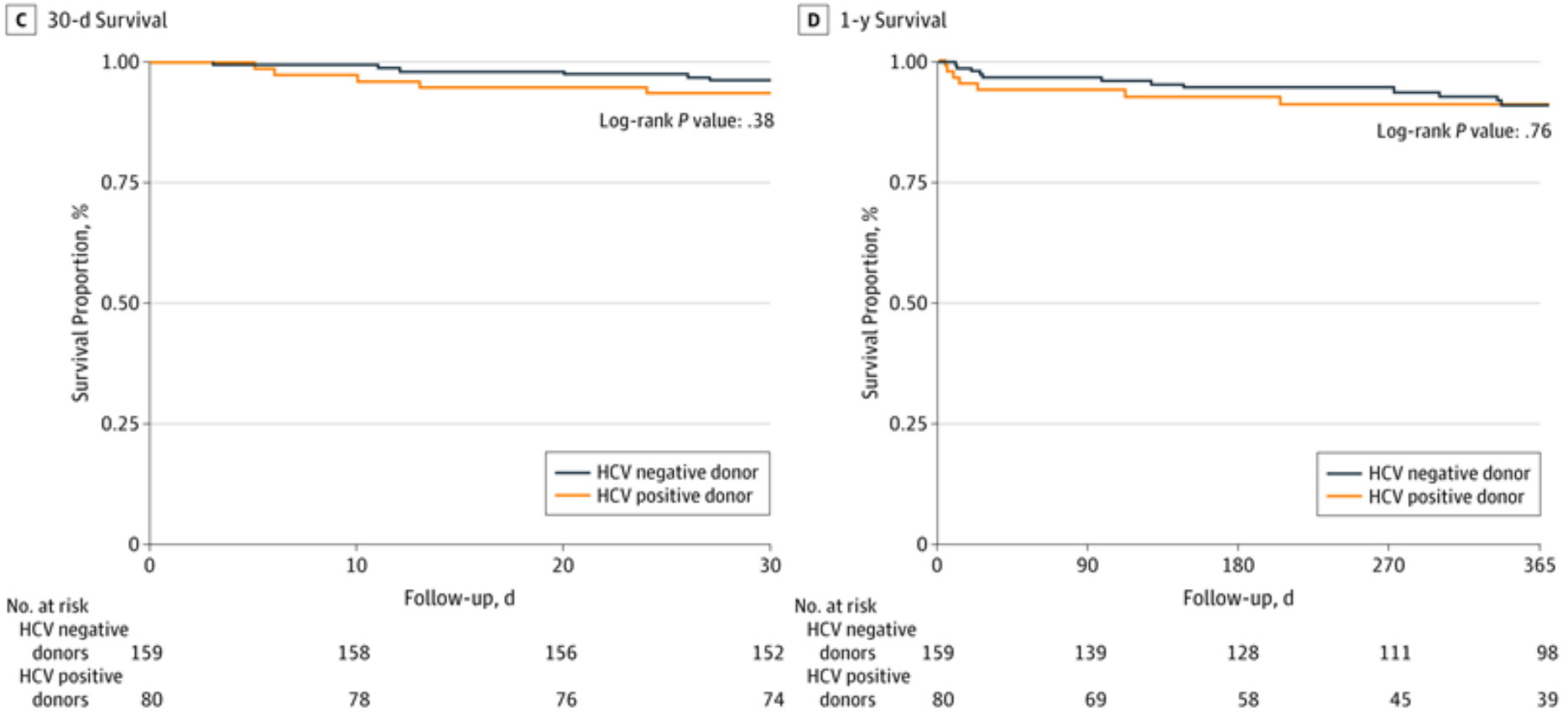
Advances in Transplant



Schlendorf et al.

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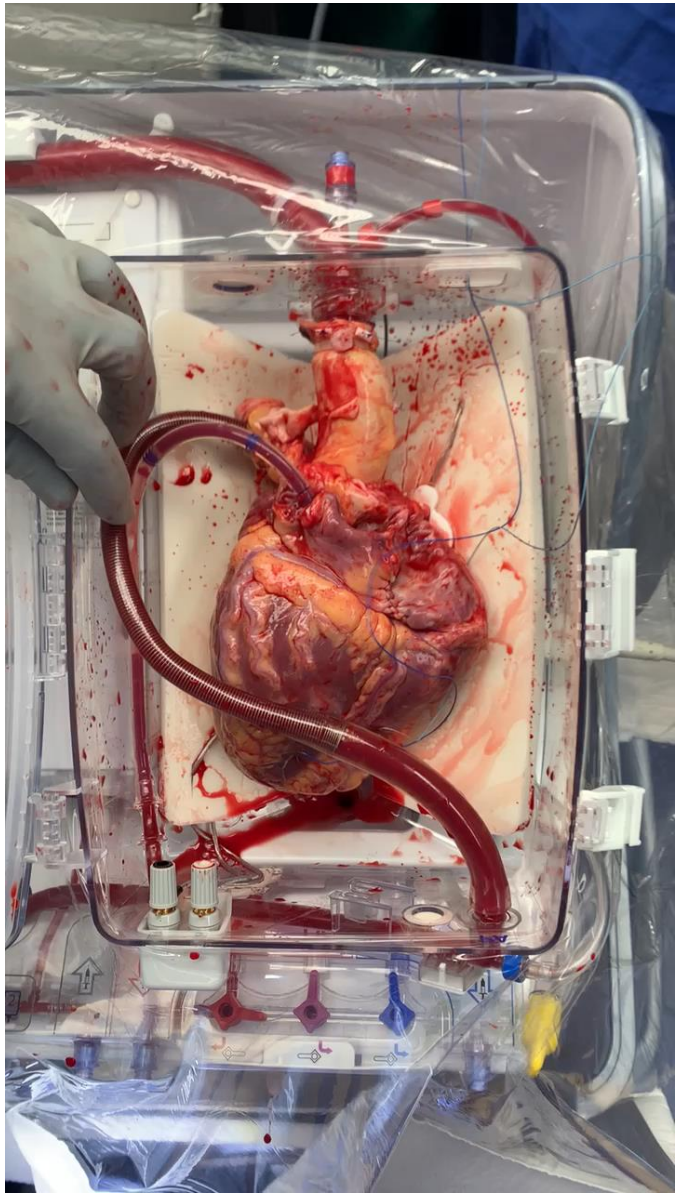
Advances in Transplant



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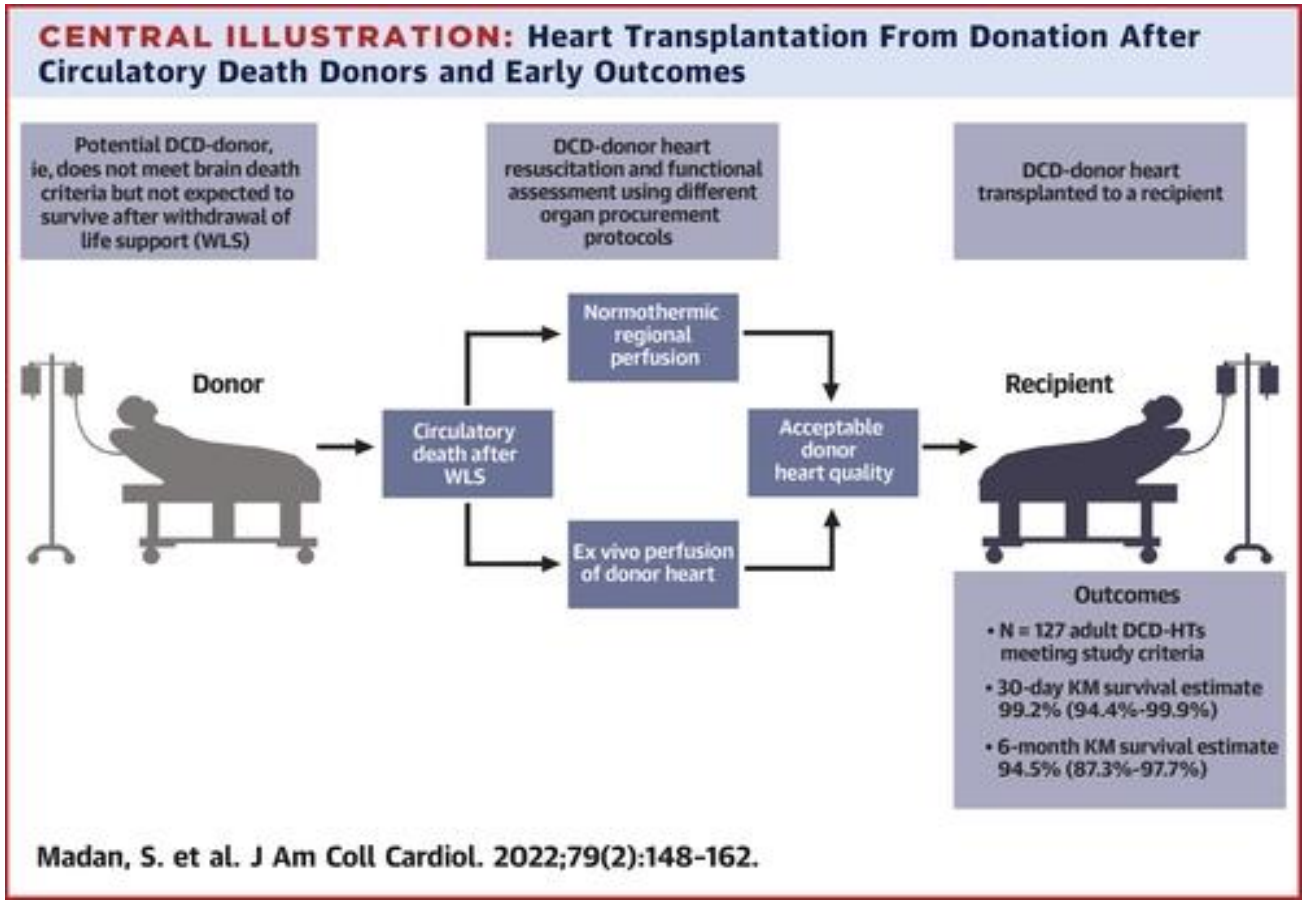

Shivank Madan et al. *J Am Coll Cardiol* 2021; 79:148-162.

2022 American College of Cardiology Foundation

JACC JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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Advances in Transplant

Table 7
Posttransplant Mortality in Propensity Matched Cohort of DCD-HT vs DBD-HT

	DCD-HT (n = 126) Cumulative KM Estimates (95% CI)	DBD-HT (n = 252) Cumulative KM Estimates (95% CI)	Unadjusted Cox HR (95% CI)	*P* Value	Adjusted Cox HR[a] (95% CI)	*P* Value
30-d mortality	0.8% (0.1%-6.5%)	3.3% (1.6%-6.5%)	0.26 (0.03-2.09)	0.206	0.11 (0.01-1.88)	0.127
6-mo mortality	5.5% (2.3%-12.7%)	6.1% (3.6%-10.5%)	0.81 (0.29-2.25)	0.688	0.47 (0.10-2.14)	0.331

DBD-HT = donation after brain death heart transplantation; DCD-HT = donation after circulatory death heart transplantation; other abbreviations as in **Table 4**.

a Propensity matched and adjusted for ischemic time.

Shivank Madan et al. *J Am Coll Cardiol* 2021; 79:148-162.

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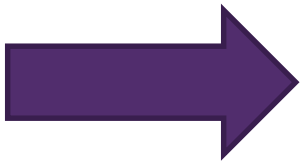
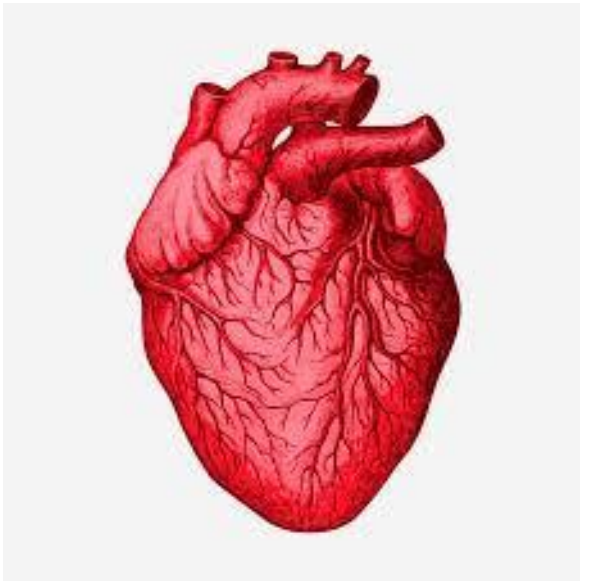
Advances in Transplant

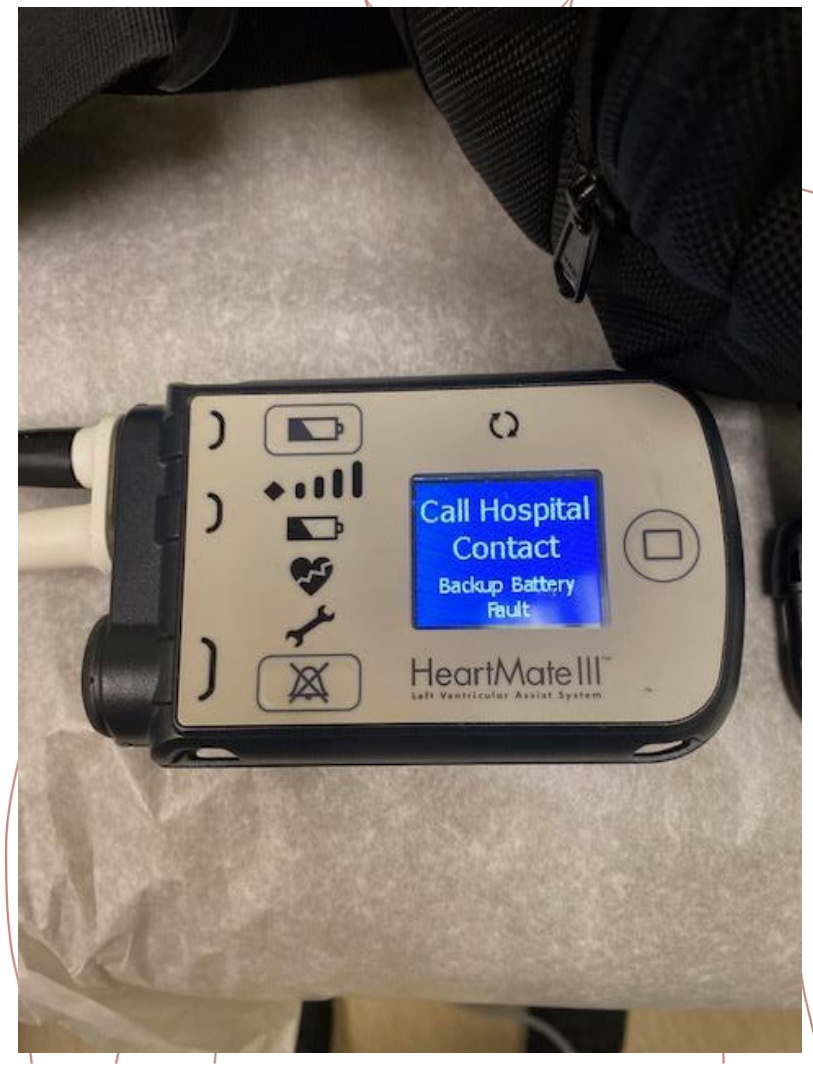




Left Ventricular Assist Device

Mechanical device used to replace or reproduce the pump function of the left and/or right ventricle

- **<u>Device Components</u>**:
  - Propulsion
  - Inflow/Outflow Cannula
  - Power Supply
  - Control Unit



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Left Ventricular Assist Device

	First-Generation	Second-Generation	Third-Generation
Flow Profile	Pulsatile	Continuous (Axial)	Continuous (Centrifugal)
Device Example	HeartMate XVE	HeartMate II	HeartWare HVAD
Device Size	1150 grams	290 grams	160 grams
Recommended Anticoagulation	Aspirin Only	Aspirin + Coumadin	Aspirin + Coumadin
Power Source	Pneumatic or Electric	Electric	Electric
Implant Site	Abdomen	Abdomen/Chest	Pericardium
Approved Indication	BTT, DT	BTT, DT	BTT

Abbreviations: BTT – bridge-to-transplant, DT – destination therapy

Katz et al.

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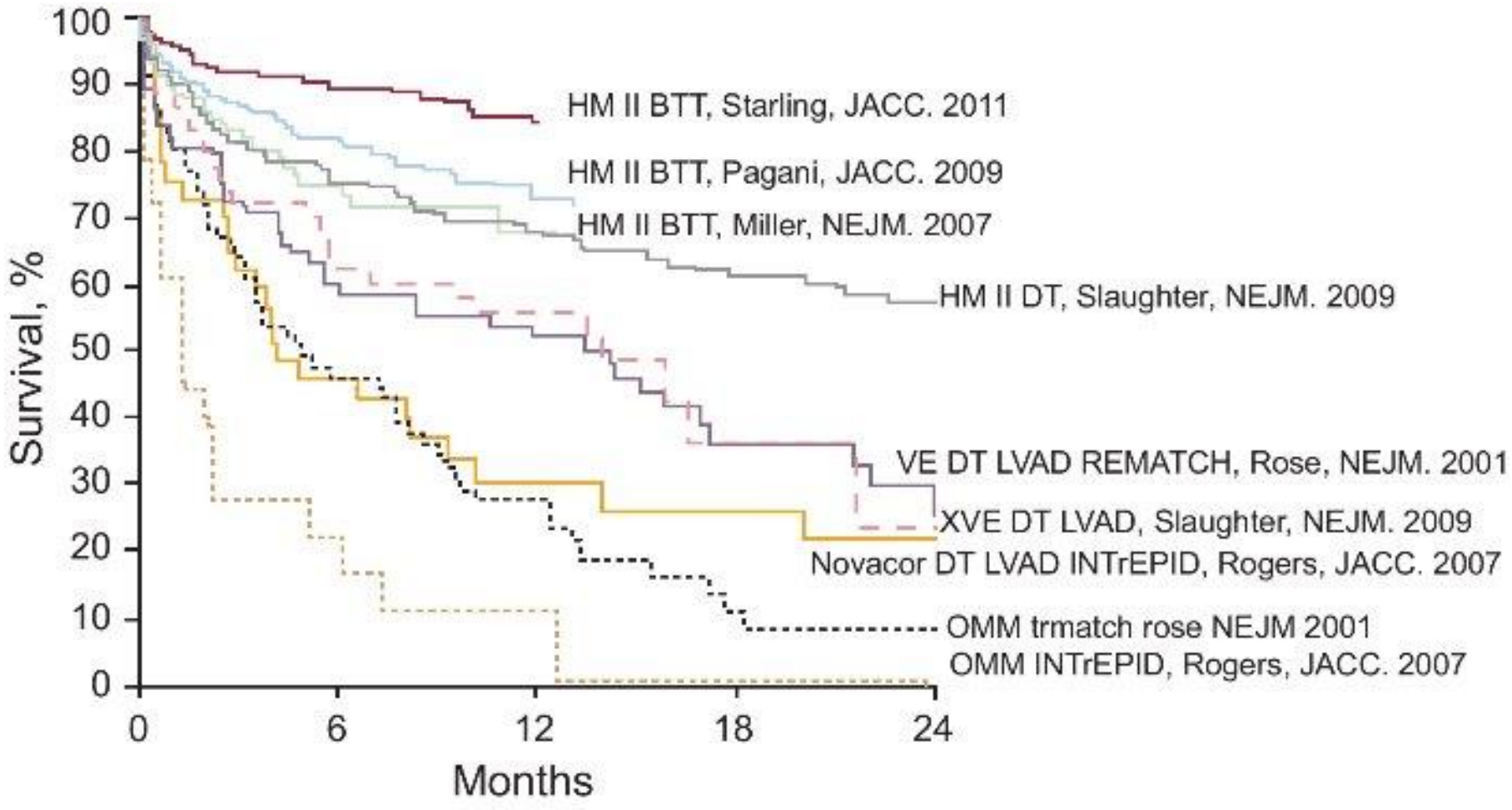
Left Ventricular Assist Device



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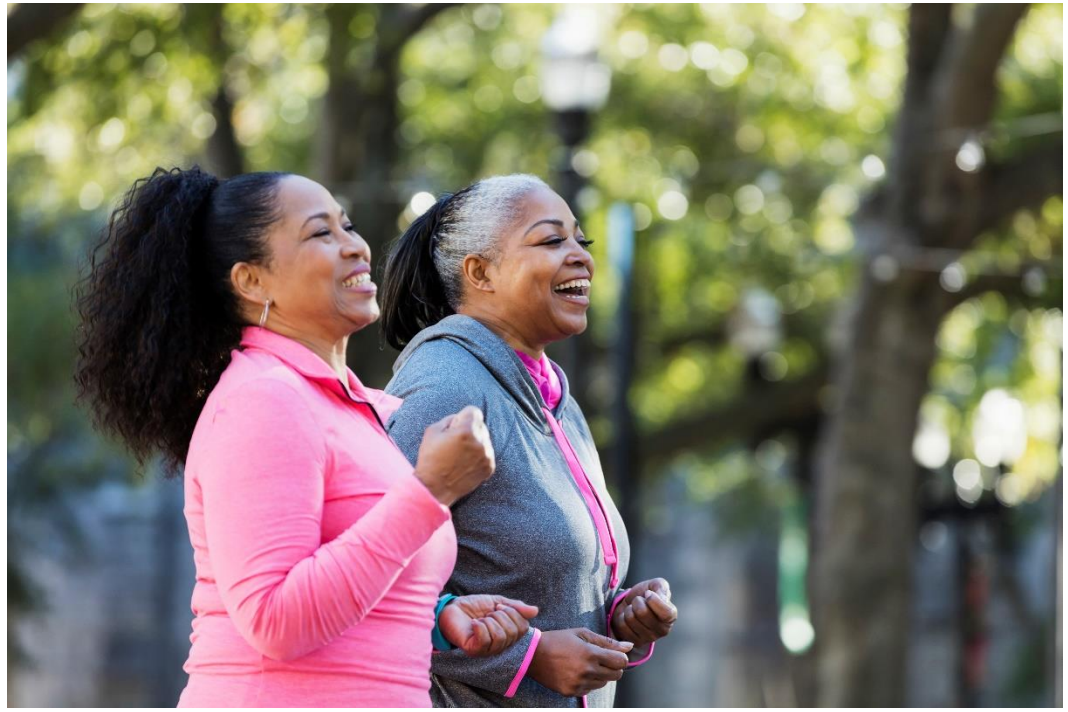
Left Ventricular Assist Device

Improvement in 6-Minute Walk

Improvement in NYHA class

Improvement in quality of life



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Left Ventricular Assist Device

ADVERSE EVENT PROFILE[1]

Adverse events through six months for patients implanted with the HeartMate 3™ LVAD (n = 151).

Device thrombosis	0	0%	0
Hemolysis not associated with pump thrombosis	1	0.7%	1
GI bleeding	24	15.9%	47
Stroke*	12	7.9%	12
Ischemic	8	5.3%	8
Hemorrhagic	4	2.6%	4
Bleeding requiring surgery	15	9.9%	15
Device malfunction requiring reoperation	1	0.7%	1
Driveline infection	18	11.9%	21
RVAD usage	4	2.6%	4

Mehra et al., NEJM, 2019

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Left Ventricular Assist Device

Abbott developing a Fully Implantable Left Ventricular Assist System (FILVAS).

Inotropes

Dobutamine	Milrinone
Beta adrenergic agonist	Phosphodiesterase inhibitor
Half life: minutes	Half life: hours
Works more centrally	Works more peripherally
Not dependent on kidney function	Dependent on kidney function
$	$$$

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Inotropes

First thought to be a viable option in 1997

Can decrease days in the hospital

Can be cost effective

Does not improve mortality

Can be used as a bridge to other therapies or as destination

ACC/AHA have given in a IIb indication for chronic use

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End of Life

https://www.flickr.com/photos/ru_boff/37915499055

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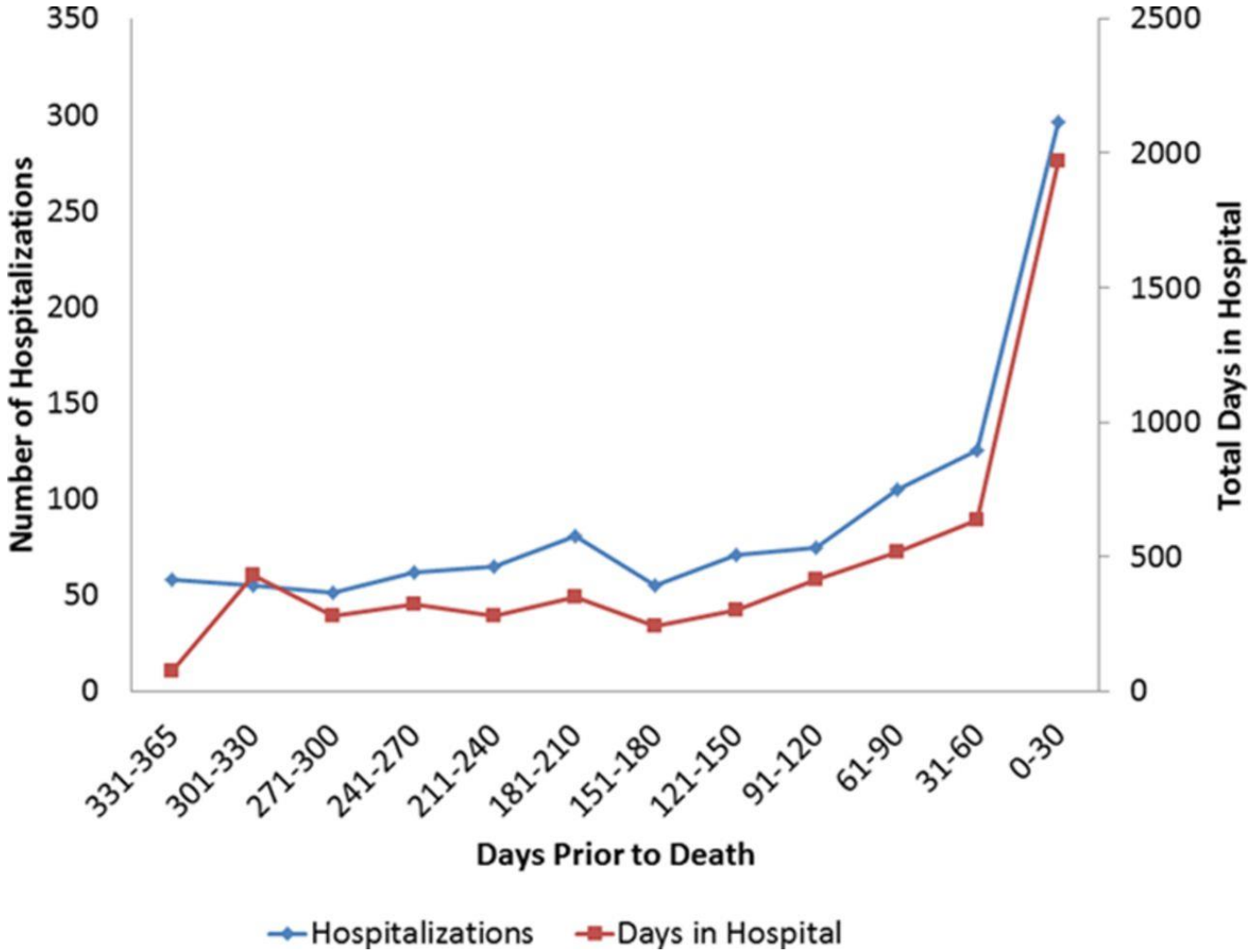
End of Life Care



Shannon M. Dunlay et al. Circ Heart Fail. 2015;8:489-496

American Heart Association.

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End of Life Care

Heart failure only accounts for 11-14% of hospice admissions

Hospice services utilized in <10% of all CHF patients

Referrals are often late in the disease course

Late referrals are associated with decreased satisfaction, increased unmet needs, decreased awareness, and a perceived lack of coordination.

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Why so hard to talk about?

Fear of “missing something”

Time constraints

The conception of “giving up”

Conversations are challenging

Limited data

Hard to identify the correct time to address

Current treatment models might not be ideal

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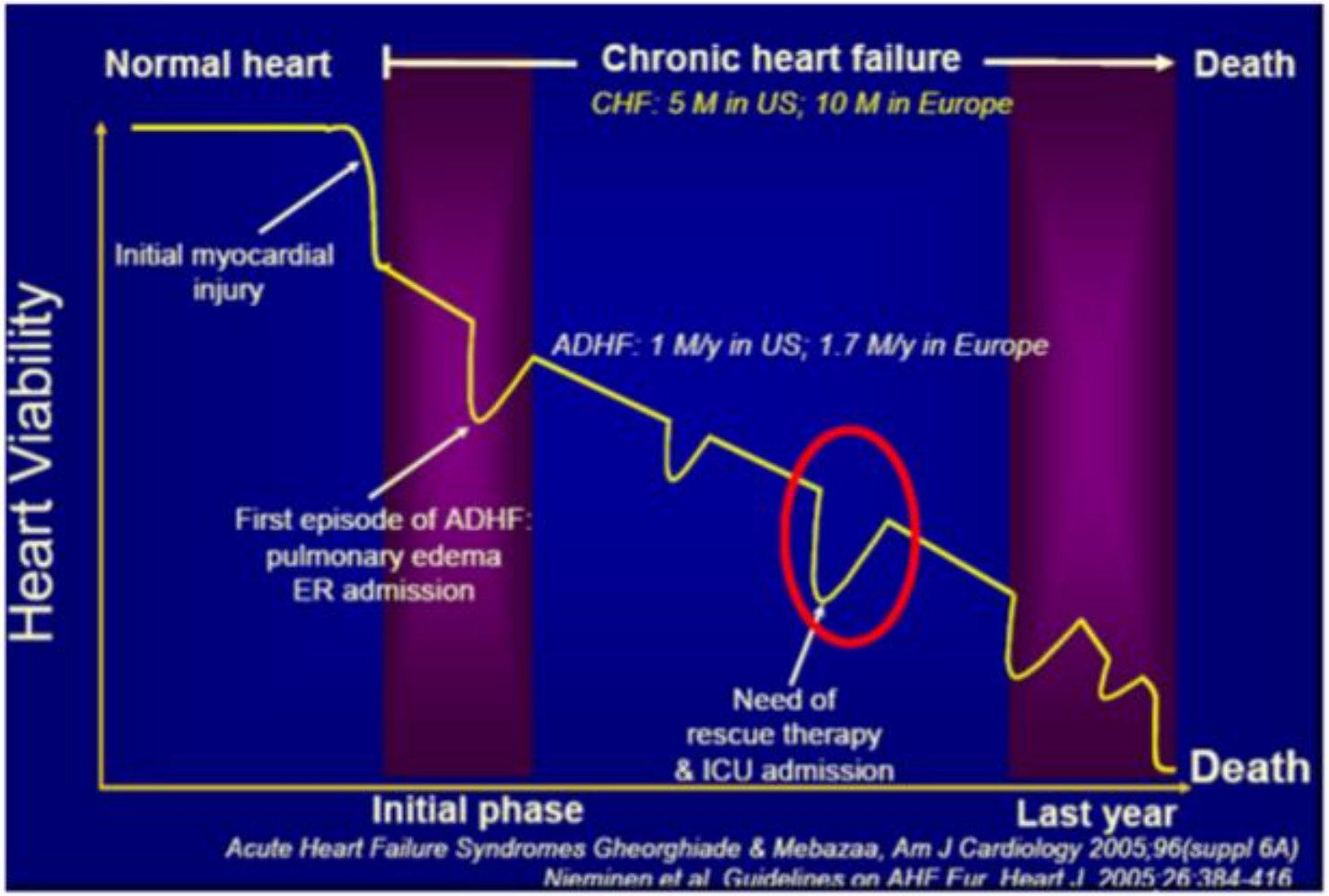
Why so hard to talk about?



Nieminem et. al

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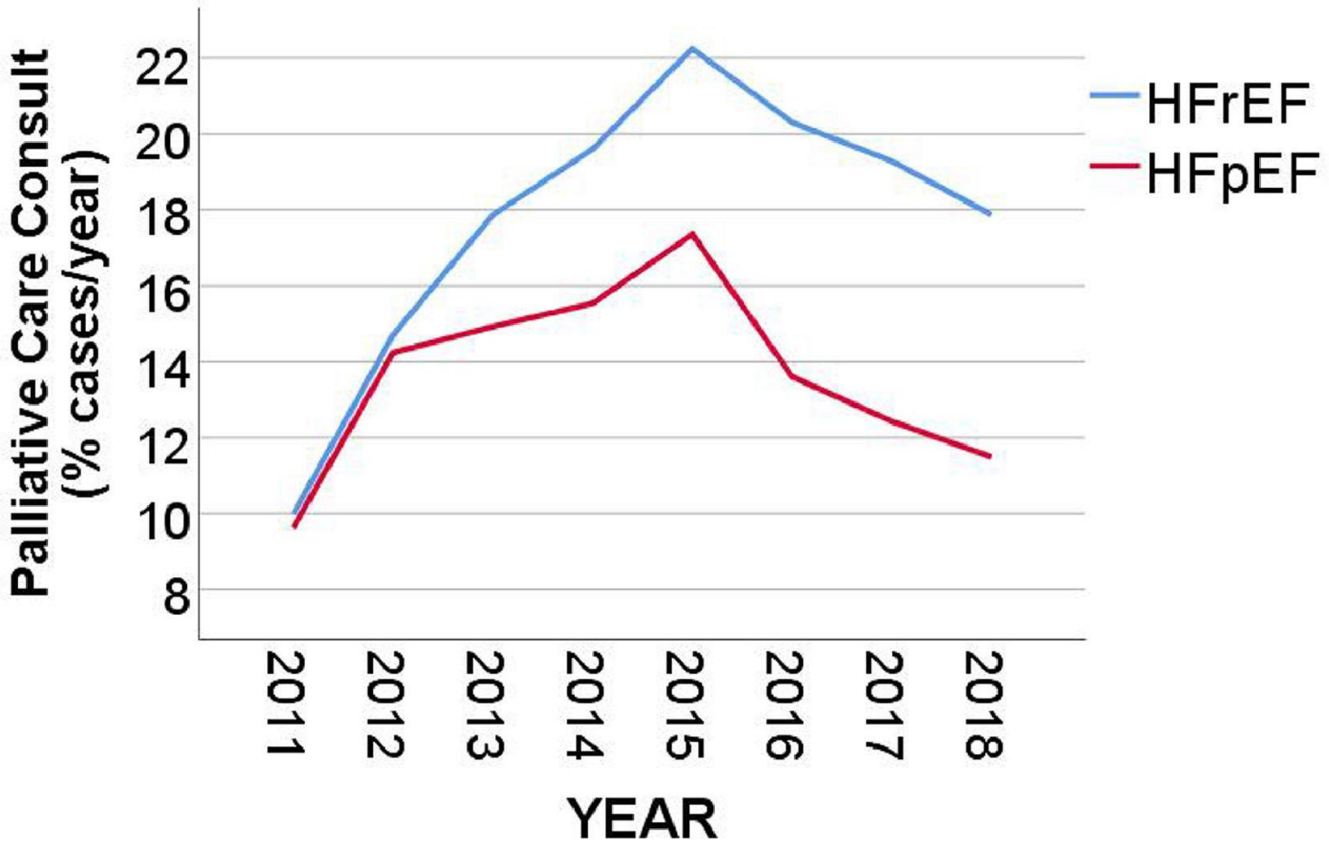

Journal of Cardiac Failure 2019 25S148-S149DOI: (10.1016

Owen et. al

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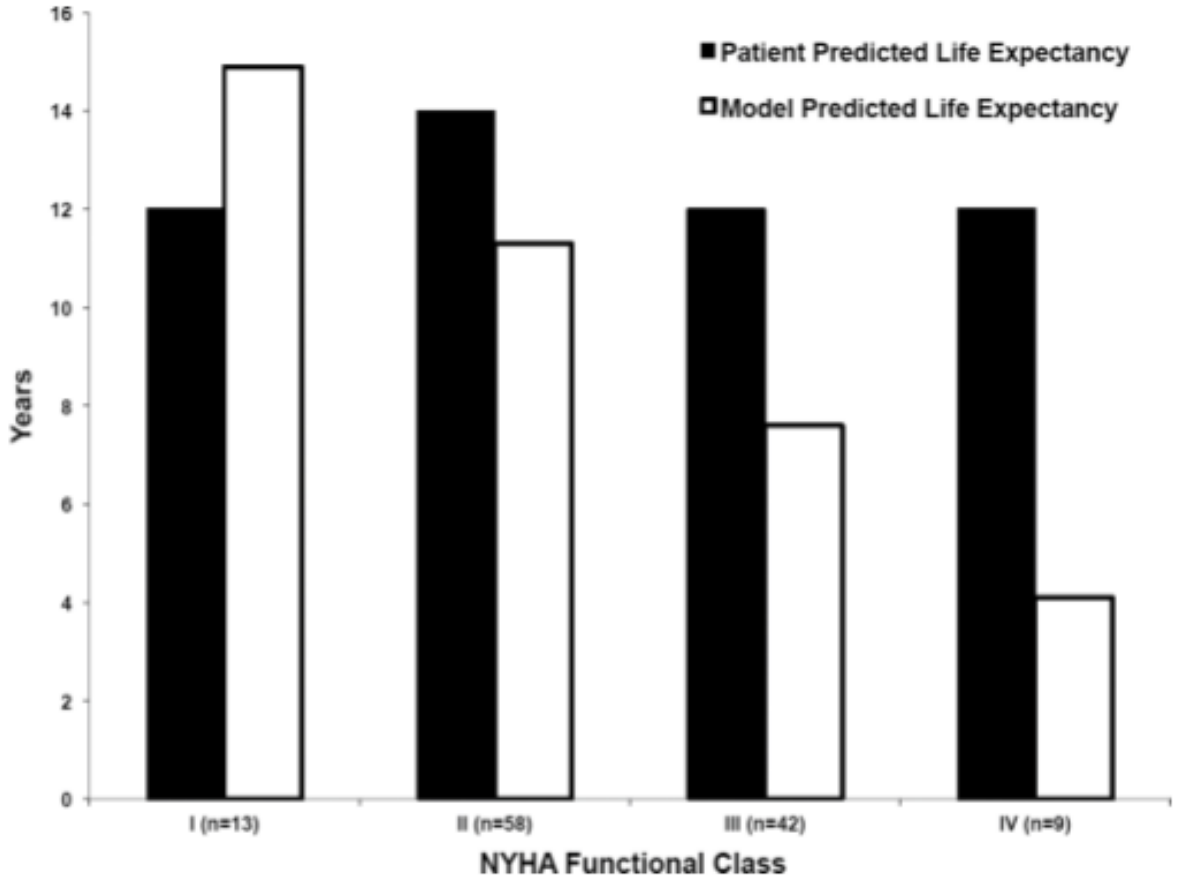

Allen et. al

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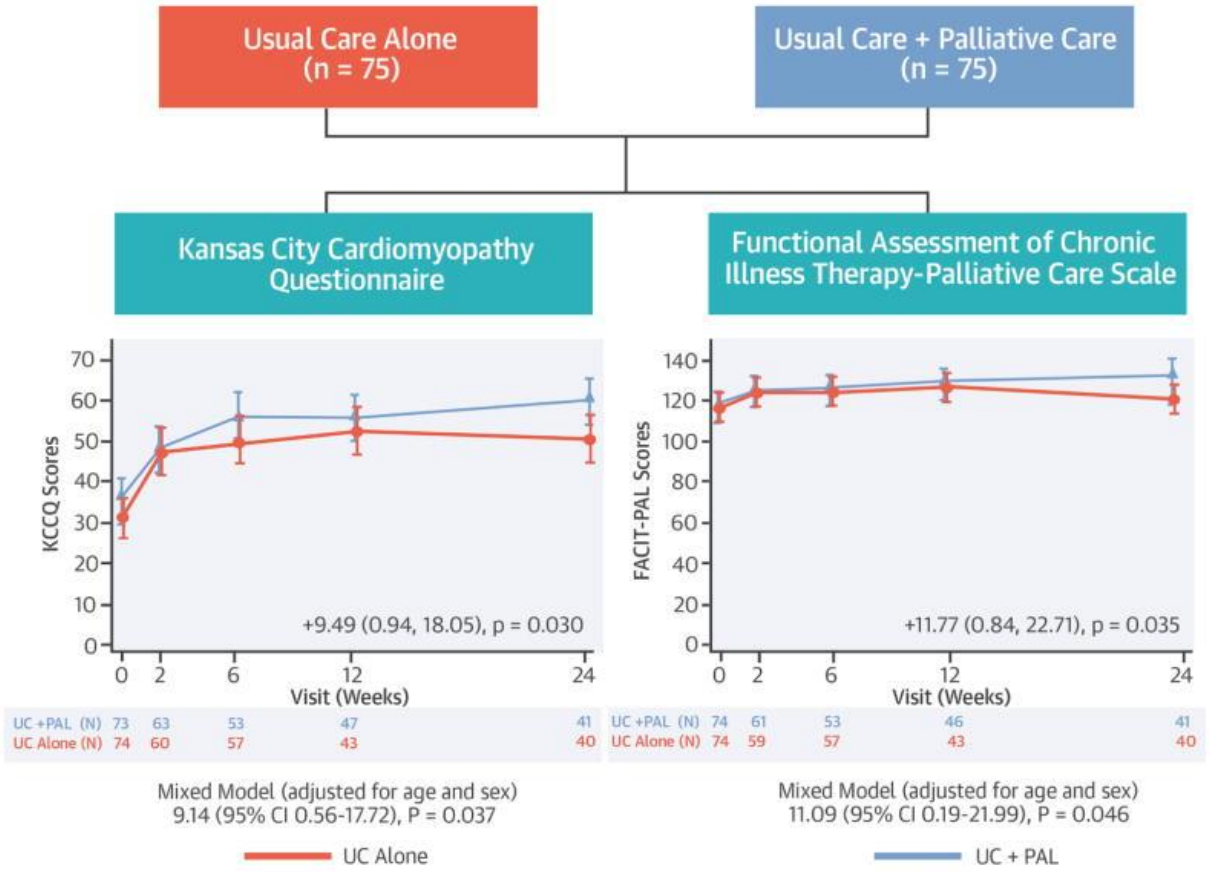
End of Life Care



Rogers et. al

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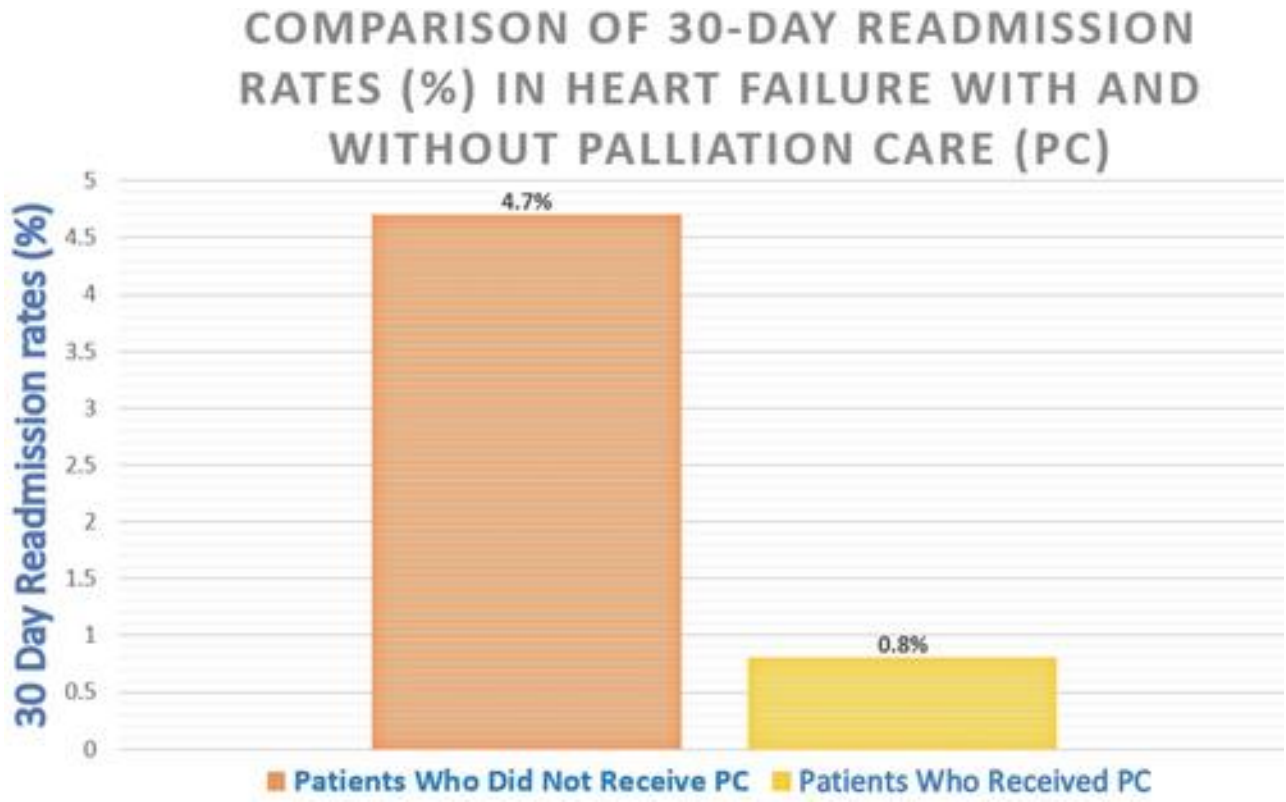
End of Life Care



Singanallur et. al

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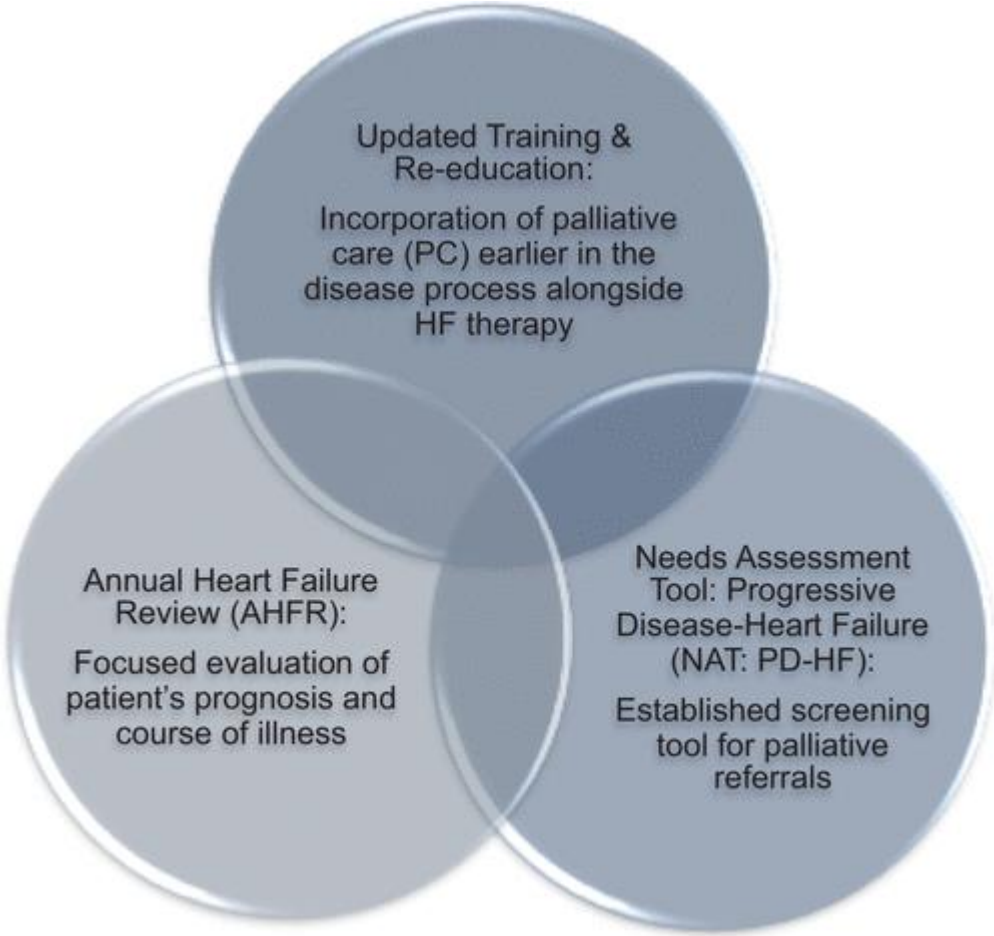
End of Life Care



Crimmins et. al

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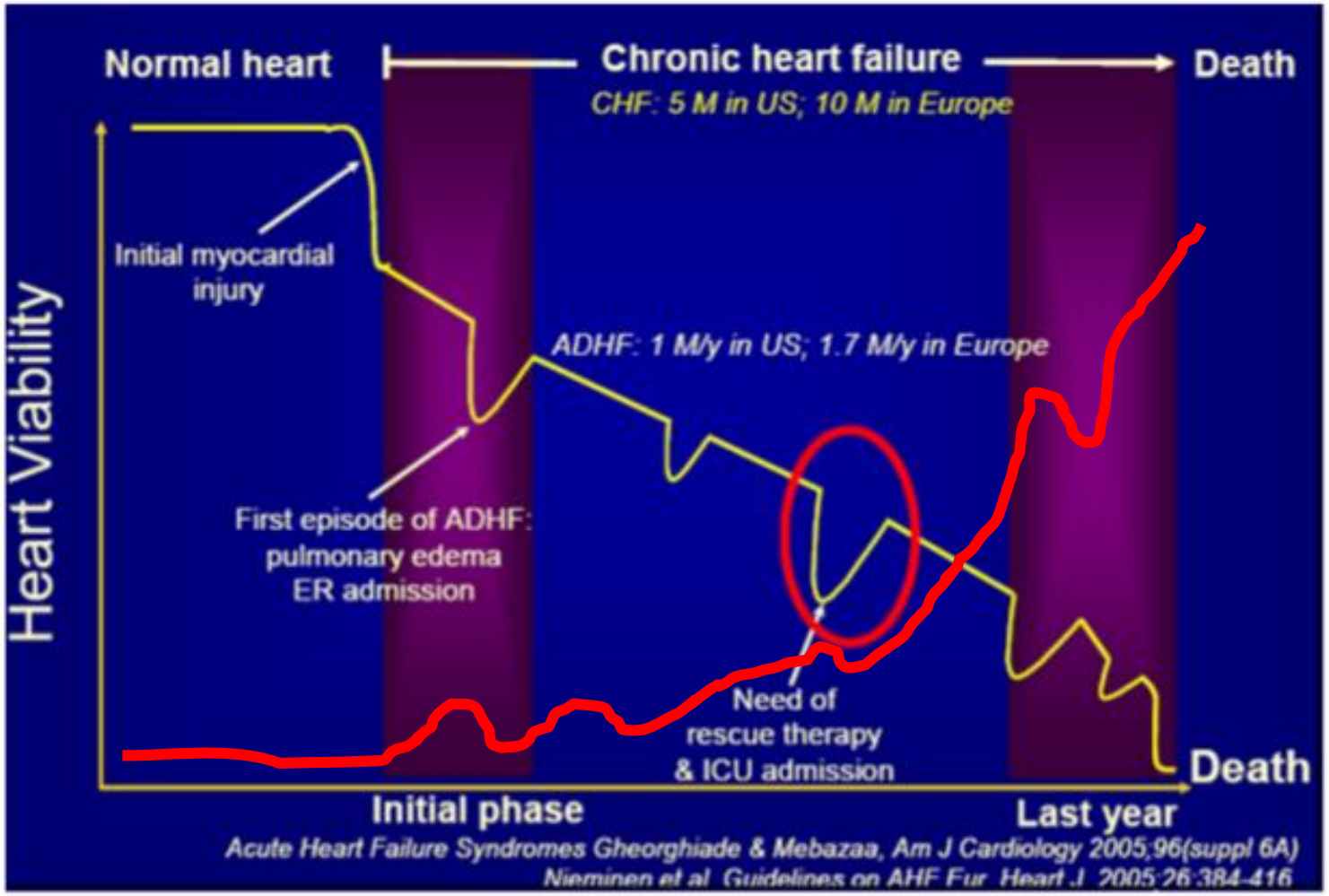
End of Life Care



Nieminem et. al

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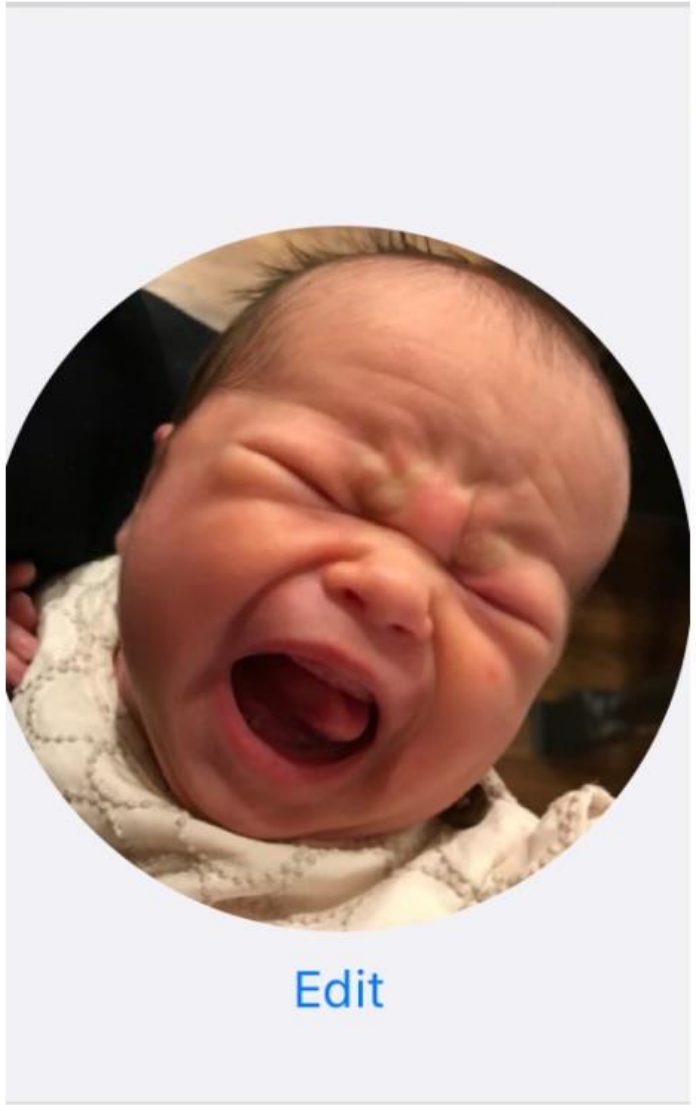
Thank you!



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