Updates in Advanced Heart Failure 2019

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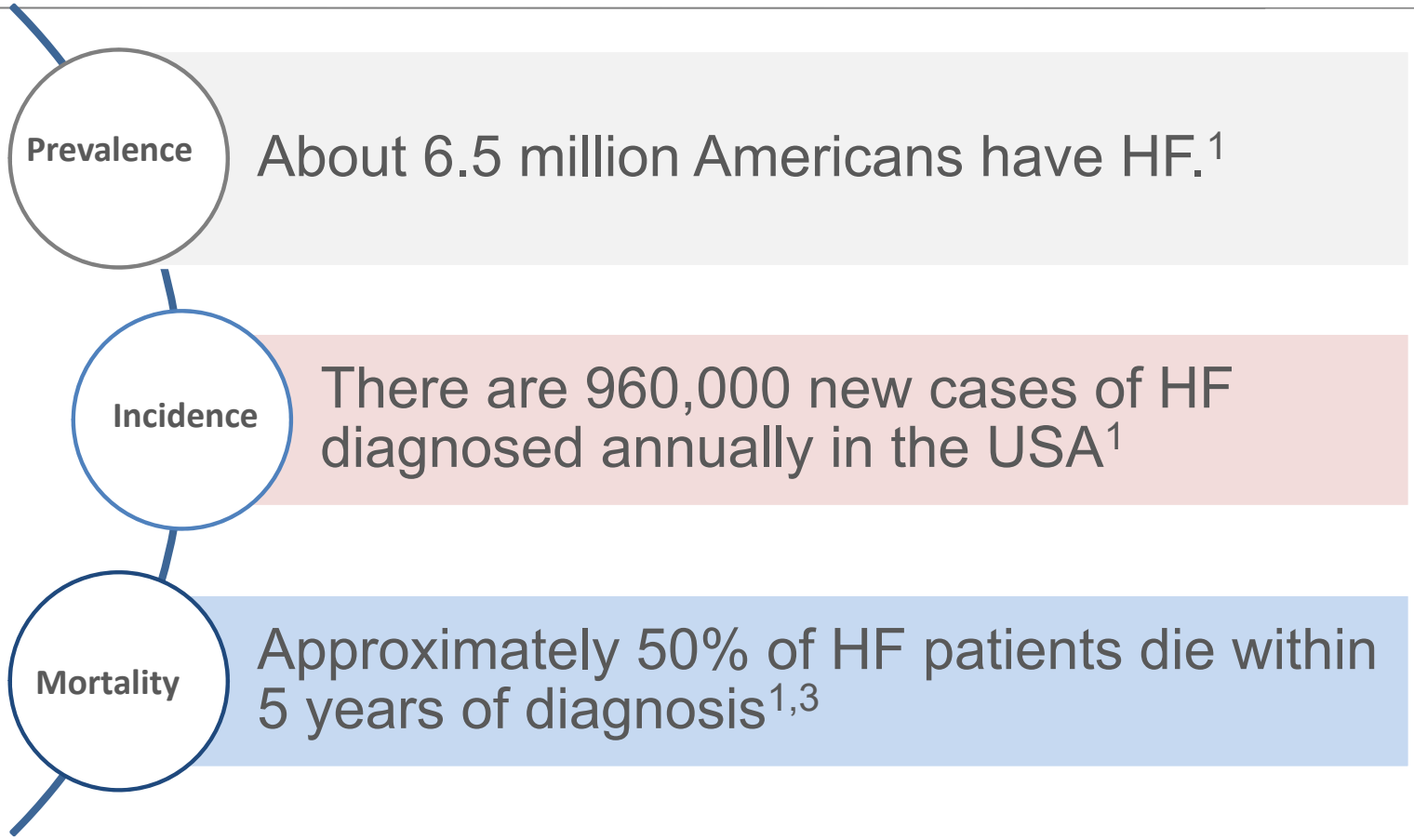
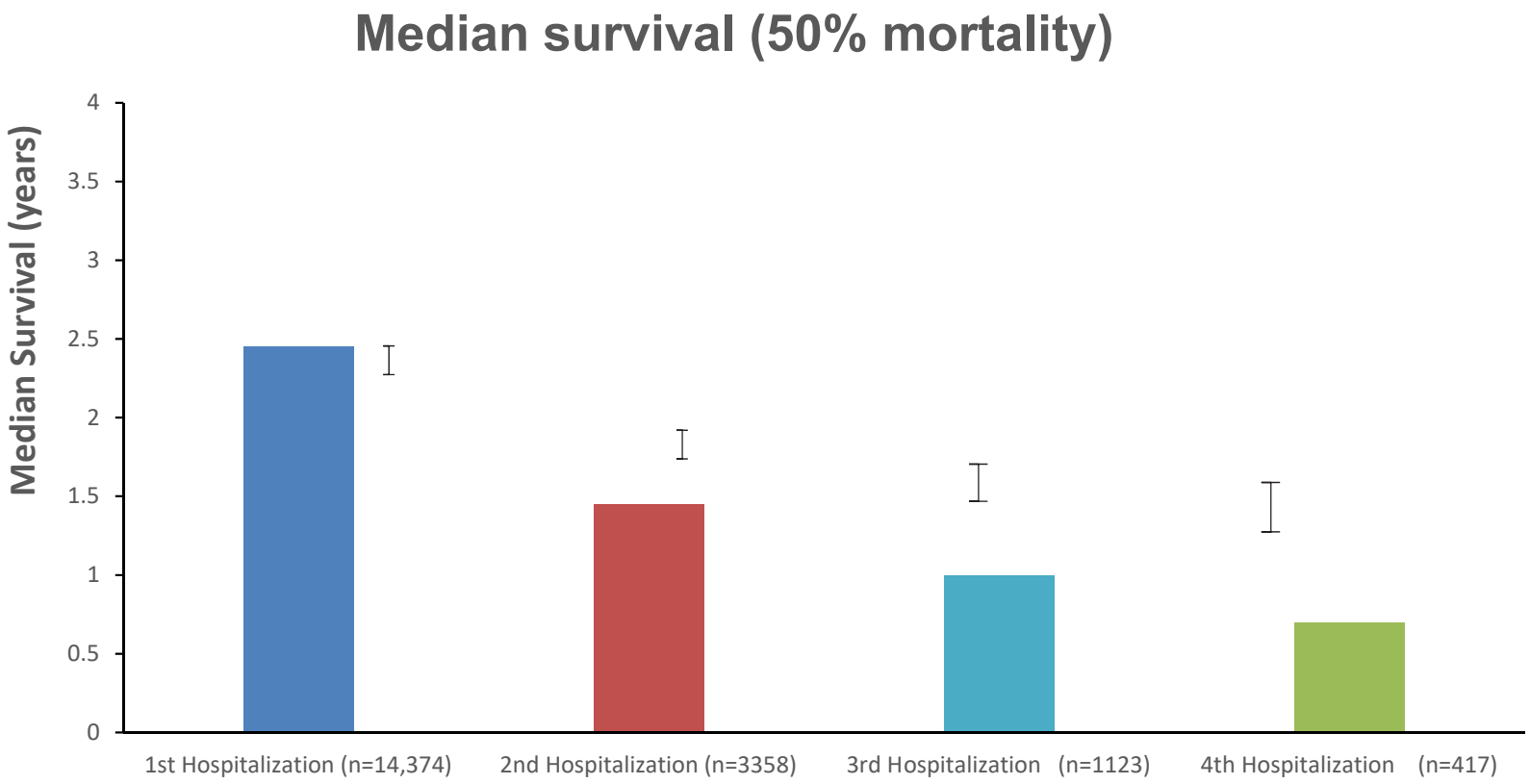
Statistics



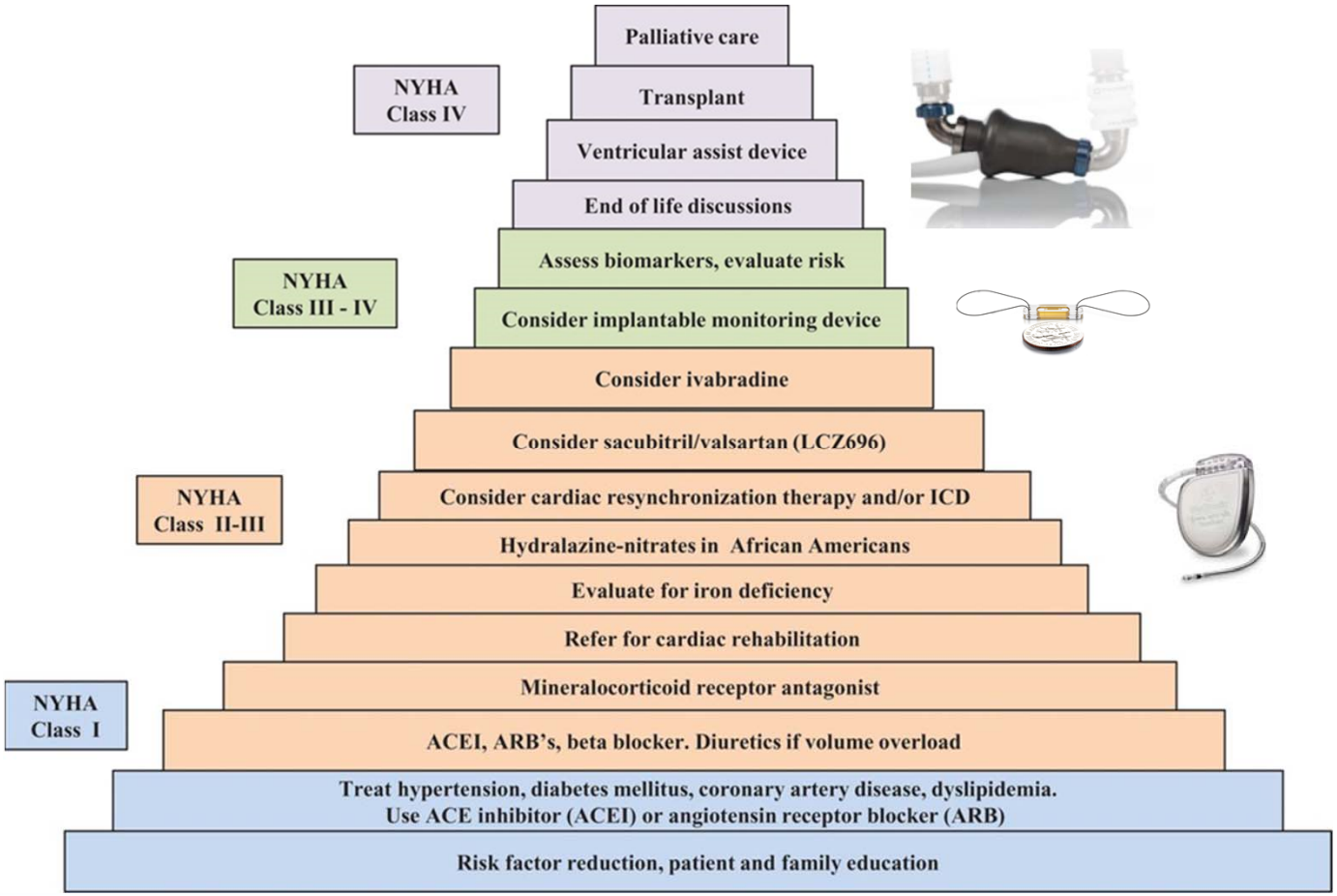
1. Benjamin et al. Circulation.2017;135:e146-603
2. Roger et al. JAMA. 2004;292:344-50

Outcomes with each hospitalization



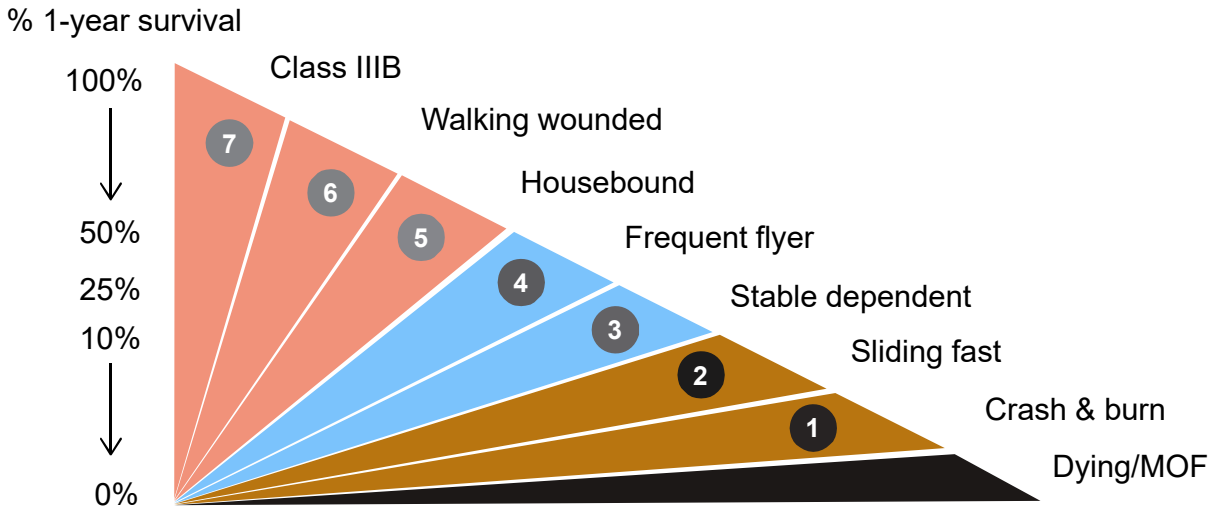
Setoguchi et al. Am Heart J. 2007;154:260-266

Approach to HFrEF



Owens et al. Circ Research 2016;118:480-495

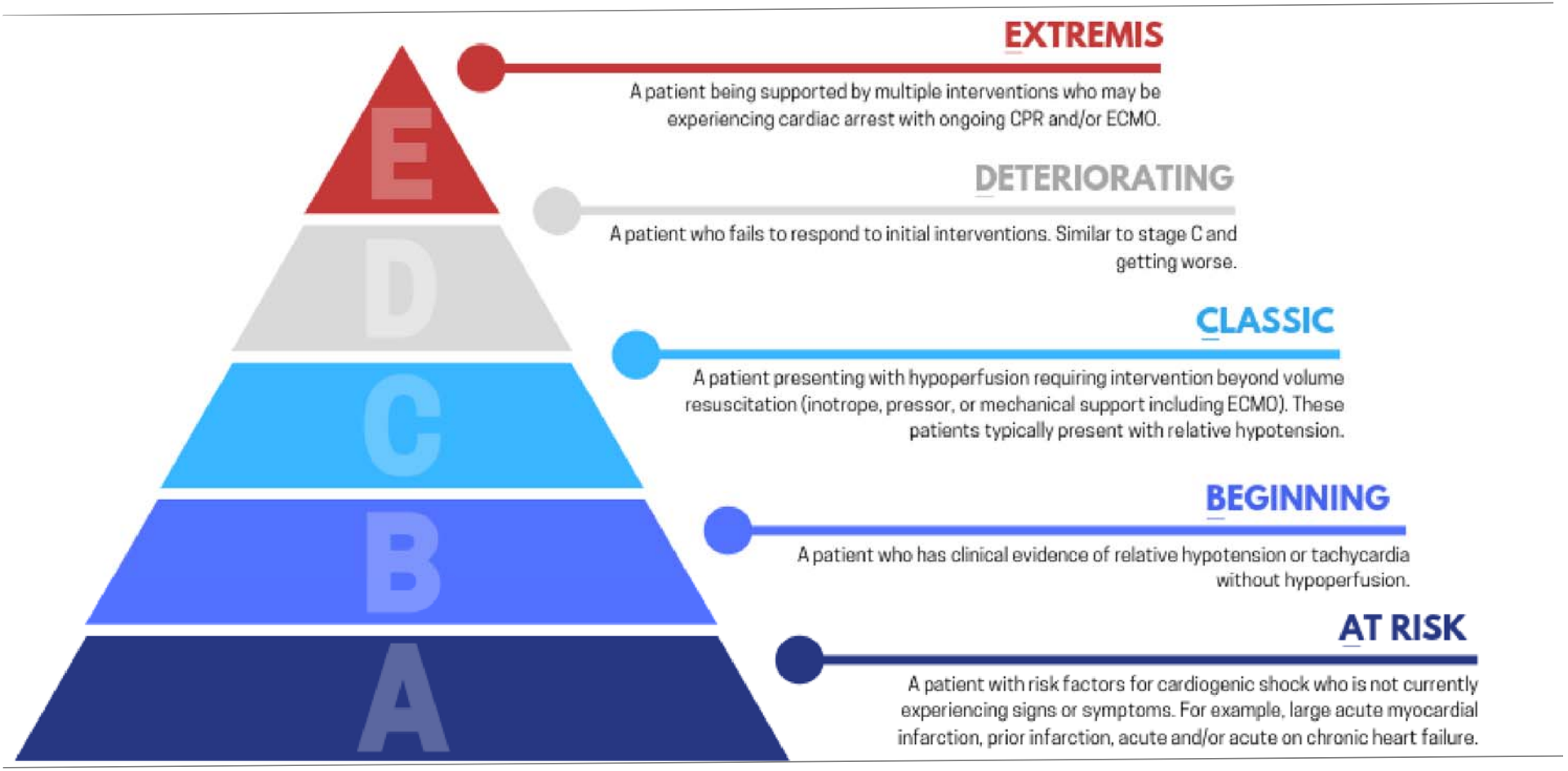
Strategies by INTERMACS Level



Intermacs level	Survival	VAD benefit
5–7	Months to years	Not established
3–4	Weeks to months	Yes
1–2	Hours to weeks	Yes
MOF	Hours to days	Bridge to decision in selected cases

INTERMACS, interagency registry for mechanically assisted circulatory support
Lietz, Miller Curr Opin Cardiol. 2009;24:246-251

New Classification of cardiac shock



Baran et al. Catheter Cardiovasc Interv 2019;94:29-37

Guidelines

- 2013 ACCF/AHA Guideline for the Management of Heart Failure
- 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure
- 2017 ACC/AHA/HFSA Focused Update Guideline for the Management of Heart Failure
- 2018 Canadian Guidelines and Australian Guidelines
- 2016 ESC Guidelines

2016 ACC/AHA/HFSA Updated Guidelines

Renin-Angiotensin System Inhibition

Recommendations for Renin-Angiotensin System Inhibition With ACE Inhibitor or ARB or ARNI		
COR	**LOE**	**Recommendations**
I	**ACE: A**	**The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors *(Level of Evidence: A)* (9-14), OR ARBs *(Level of Evidence: A)* (15-18), OR ARNI *(Level of Evidence: B-R)* (19) in conjunction with evidence-based beta blockers (20-22), and aldosterone antagonists in selected patients (23, 24), is recommended for patients with chronic HF*r*EF to reduce morbidity and mortality.**
	ARB: A	
	ARNI: B-R	
I	**ARNI: B-R**	**In patients with chronic symptomatic HF*r*EF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality (19).**

ARNI: angiotensin receptor neprilysin inhibitors

Yancy, et al. JACC 27(13):1476-88

Guidelines

2017 ACC/AHA/HFSA
Focused Update Guideline for the Management of Heart Failure

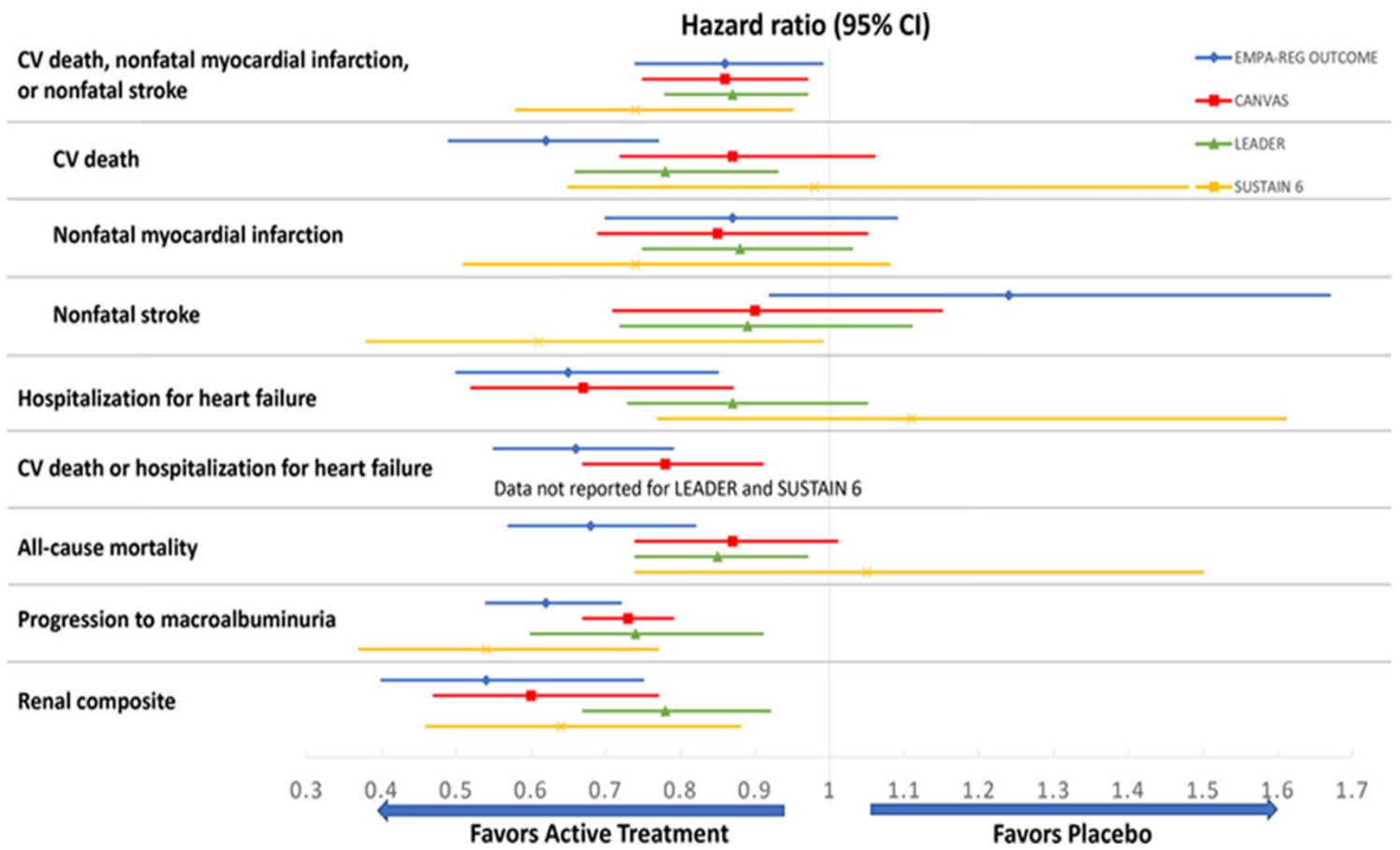
1. Biomarkers
2. New therapies indicated for stage C HF with reduced ejection fraction (HFrEF)
3. Updates on HF with preserved ejection fraction (HFpEF)
4. New data on important comorbidities, including sleep apnea, anemia, and hypertension
5. And new insights regarding the prevention of HF

Yancy et al. JACC 2017 8:70(6):776-803

Top Clinical Trials in Heart Failure 2019

1. SGLT-2 inhibitors in HFrEF
2. Transcatheter mitral valve repair for functional mitral regurgitation
3. Magnetically levitated circulatory pump for advanced heart failure
4. Tafamidis in ATTR amyloid cardiomyopathy
5. Cardiac Contractility modulation in HFrEF
6. Sacubitril-valsartan therapy in acute heart failure and HFpEF
7. Atrial fibrillation in heart failure
8. Hospital readmission reduction program increases HF mortality
9. Rivaroxaban in HFrEF without atrial fibrillation
10. Intra-atrial shunting device for HFpEF

Sodium Glucose Cotransporter-2 Inhib in HF



Lyvtyn et al. Circulation 2017:136 (17):1643-58

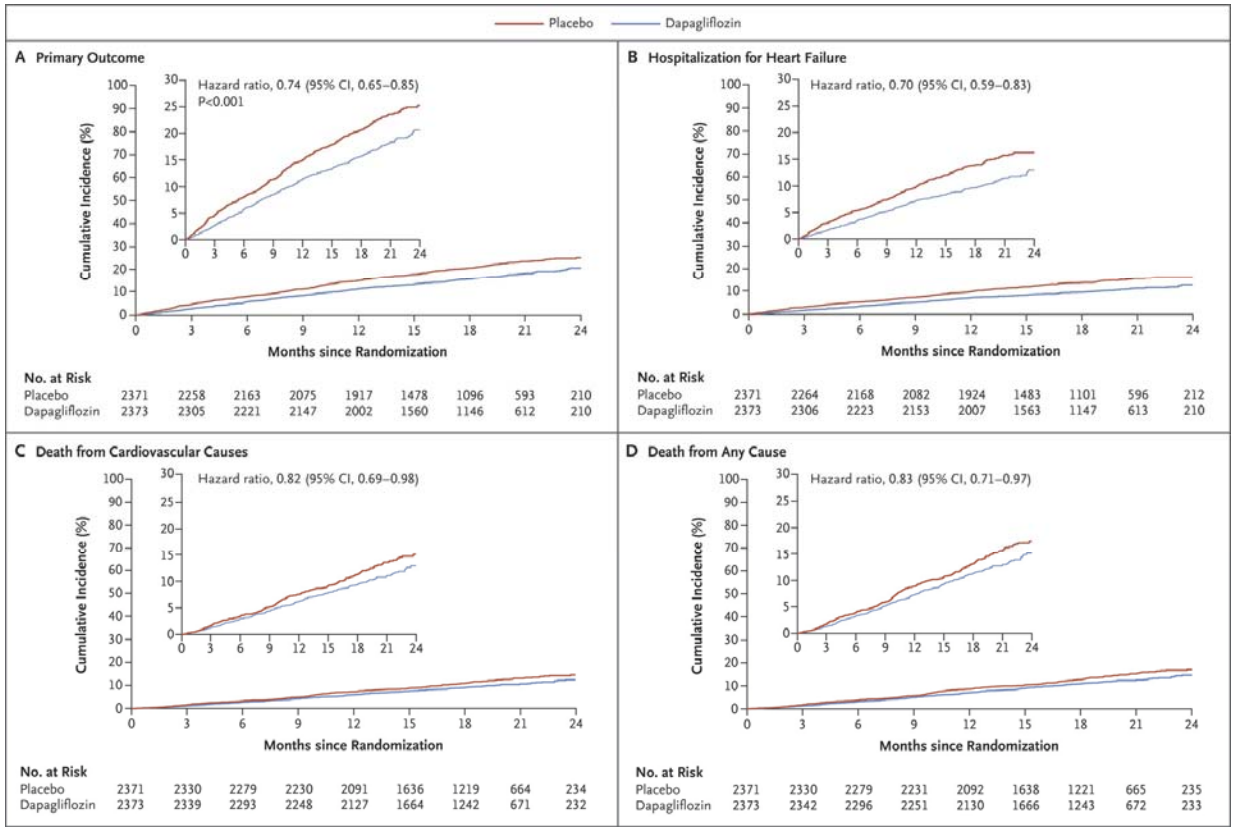
Clinical Trials: Dapa HF

Dapagliflozin vs with placebo in HFrEF.

Dapagliflozin 10 mg daily (2,373) versus placebo (2,371).

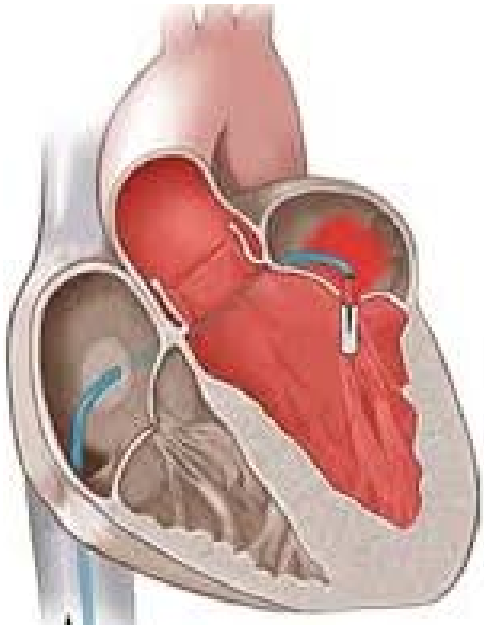
Primary outcome of cardiovascular death, hospitalization for HF, or urgent HF visit:

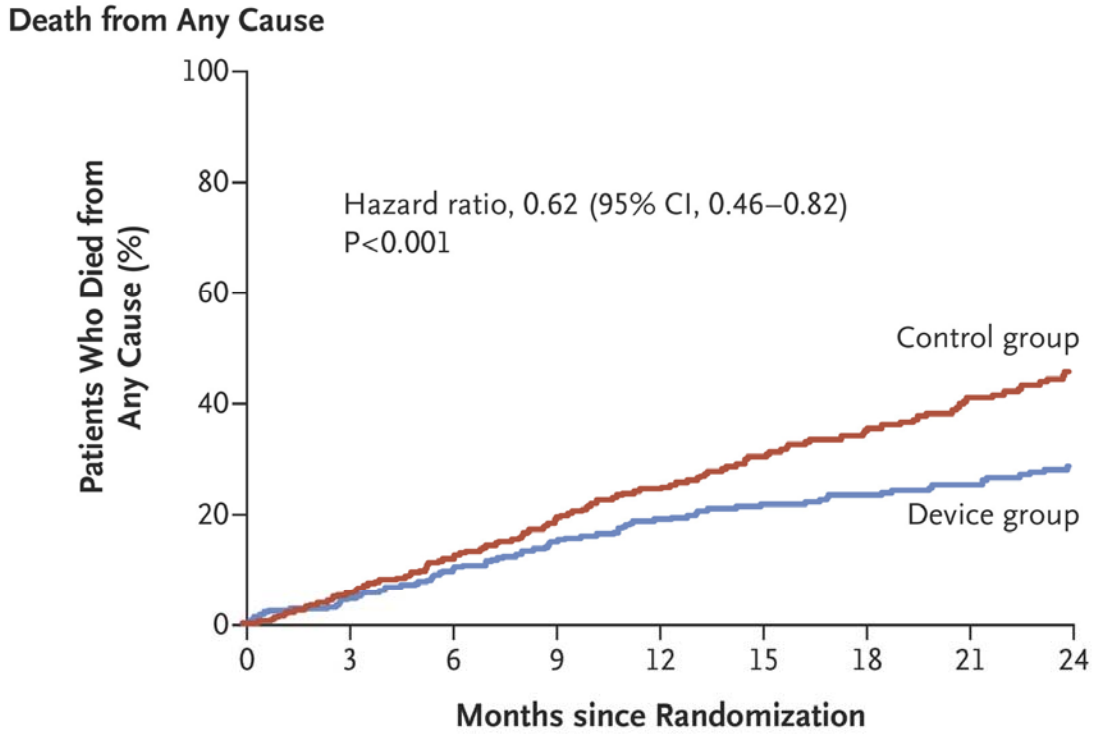
16.2% of the dapagliflozin group vs with 21.2% of the placebo group (p = 0.00001)



McMurray et al. NEJM. Sept 19, 2019

Clinical Trials: Mitral Clip



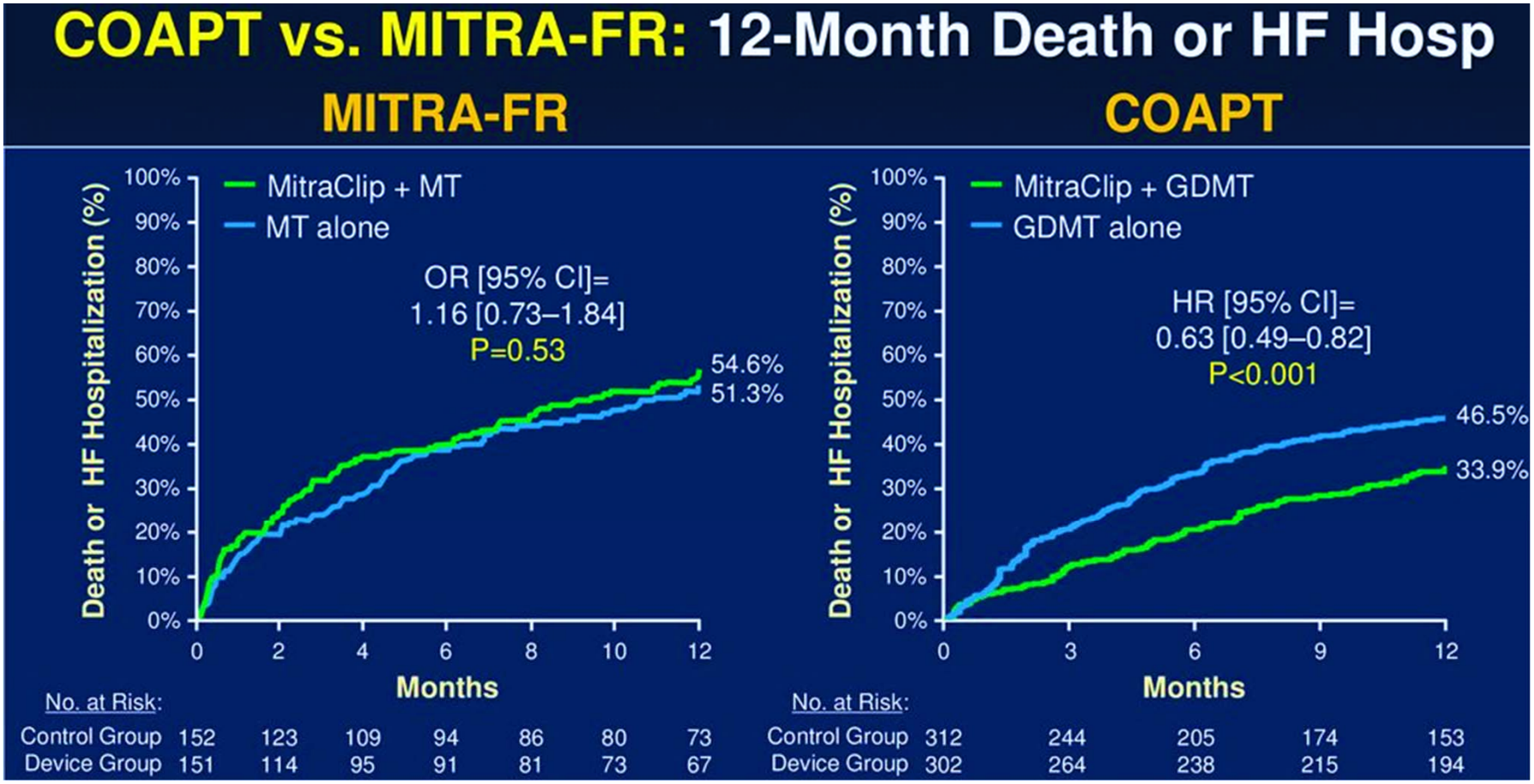


No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

Stone et al. NEJM Sept 2018; 379:2307-2318

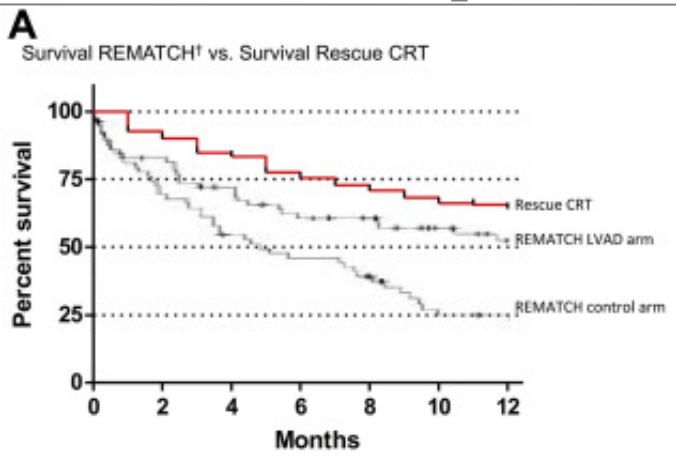
Clinical Trials: Mitral Clip

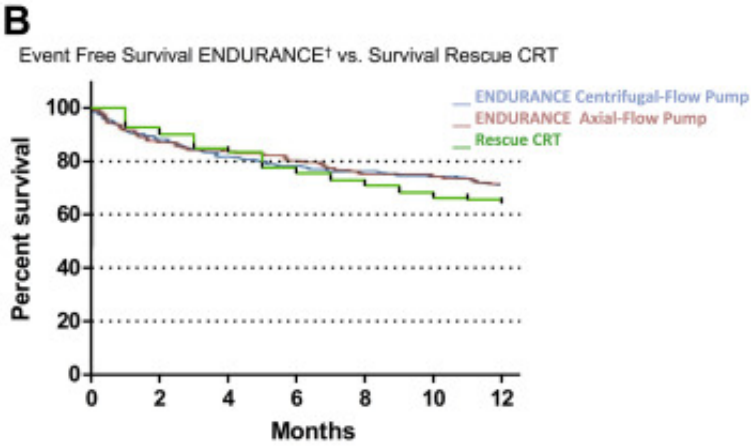


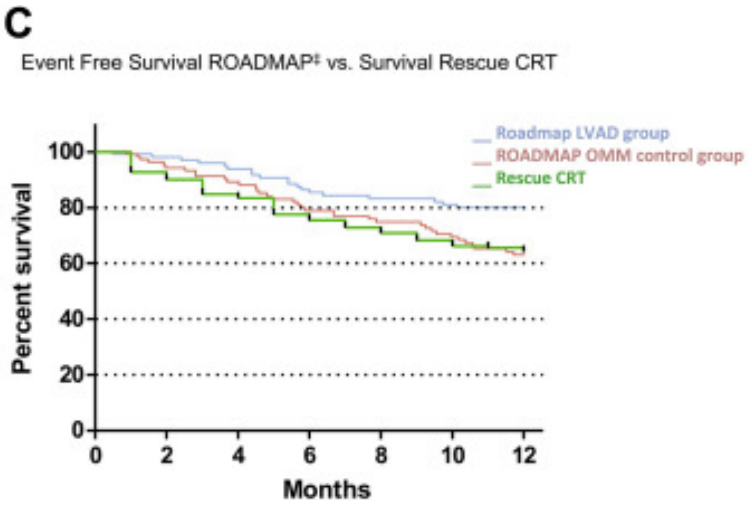
Obadia JF et al. NEJM Aug 2018; 379:2297-2306

Stone, et al. NEJM Sept 2018; 379:2307-2318

CRT in Inotrope dependent patients







Hernandez et al. JACC HF 2018 Sep;6(9)734-42

Clinical Trial: Tafamidis in TTR

Amyloidosis Cardiomyopathy

Transthyretin amyloid (TTR)
Tafamidis binds to the TTR preventing tetramer dissociation and amyloidogenesis.

Lower all-cause mortality and cardiovascular related hospitalization and improve QOL

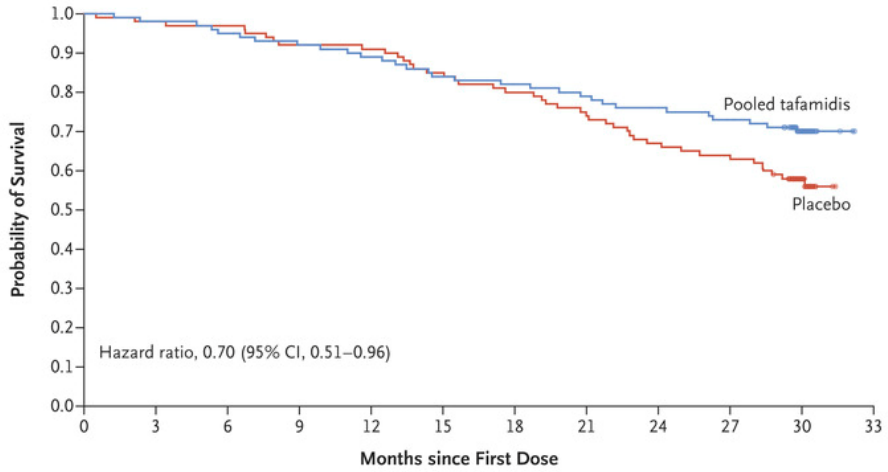
Maurer et al. NEJM Sep 13:379(11):1007-16

Clinical Trial: Tafamidis in TTR

A Primary Analysis, with Finkelstein–Schoenfeld Method

	No. of Patients	P Value from Finkelstein–Schoenfeld Method	Win Ratio (95% CI)	Patients Alive at Mo 30 *no. (%)*	Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30 *per patient per yr*
Pooled Tafamidis	264	<0.001	1.70 (1.26–2.29)	186 (70.5)	0.30
Placebo	177			101 (57.1)	0.46

B Analysis of All-Cause Mortality

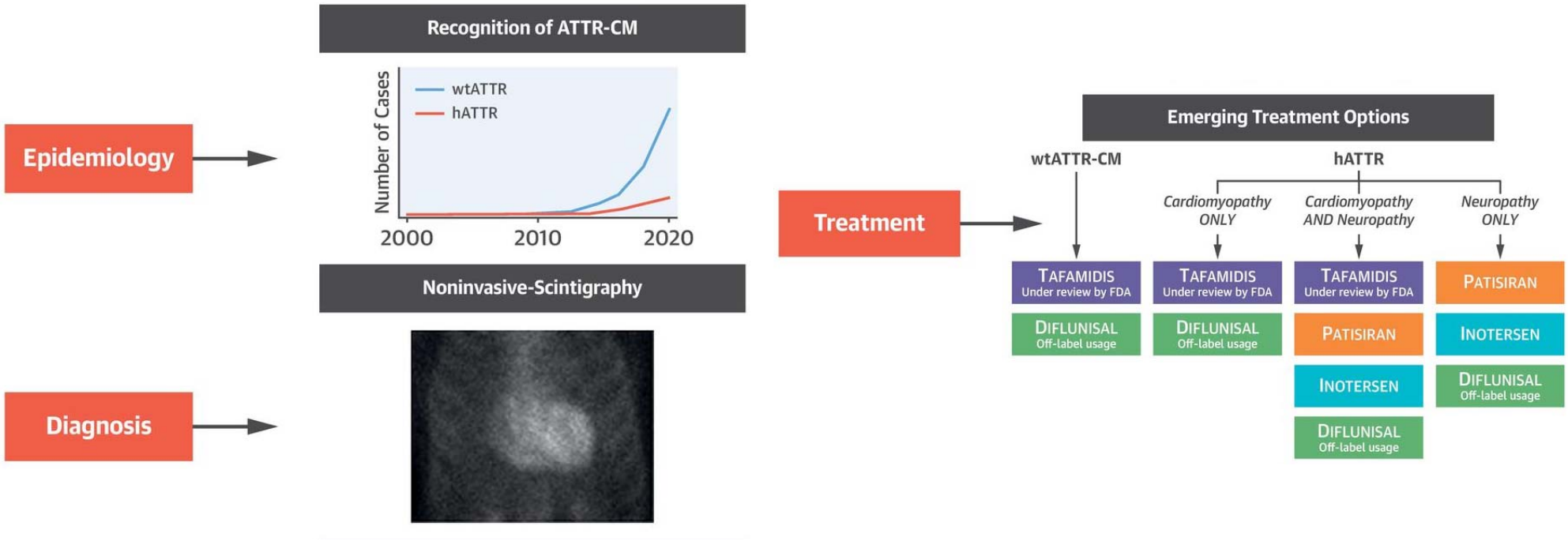


No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

Maurer et al. NEJM Sep 13:379(11):1007-16

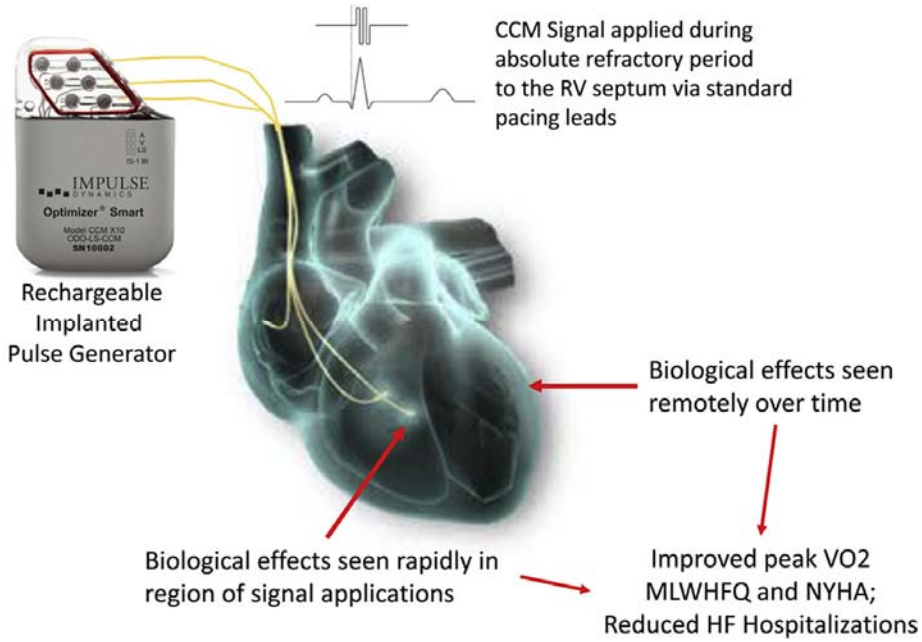
Transthyretin Cardiac Amyloidosis

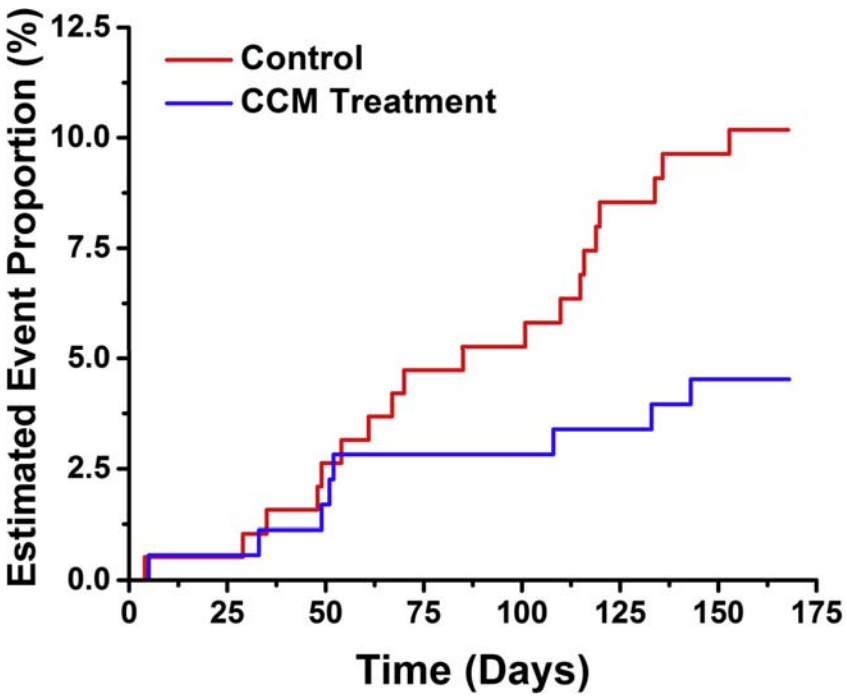


Ruberg et al. JACC 2019;73(22):2872-91

Clinical Trials: FIX HF

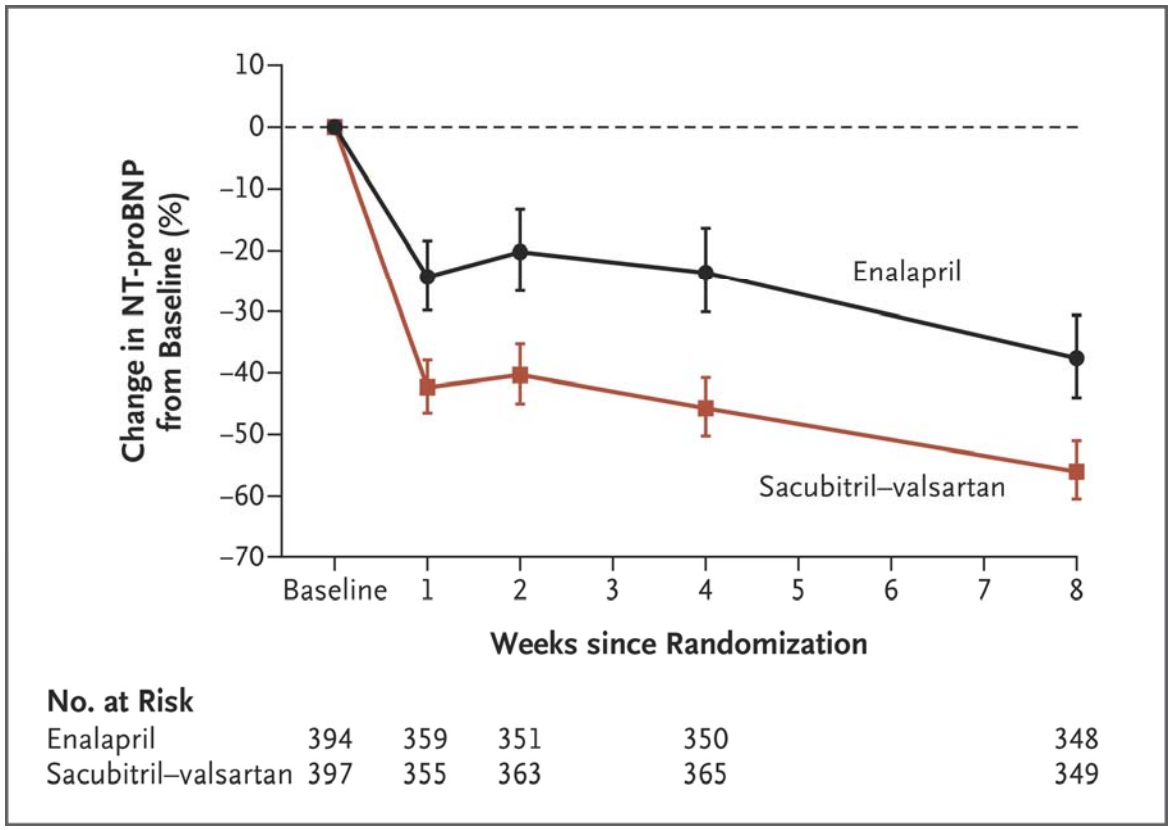
Cardiac Contractility Modulation (Optimizer Device)
166 patients with EF between 25 and 45%
NYHA 3 and 4





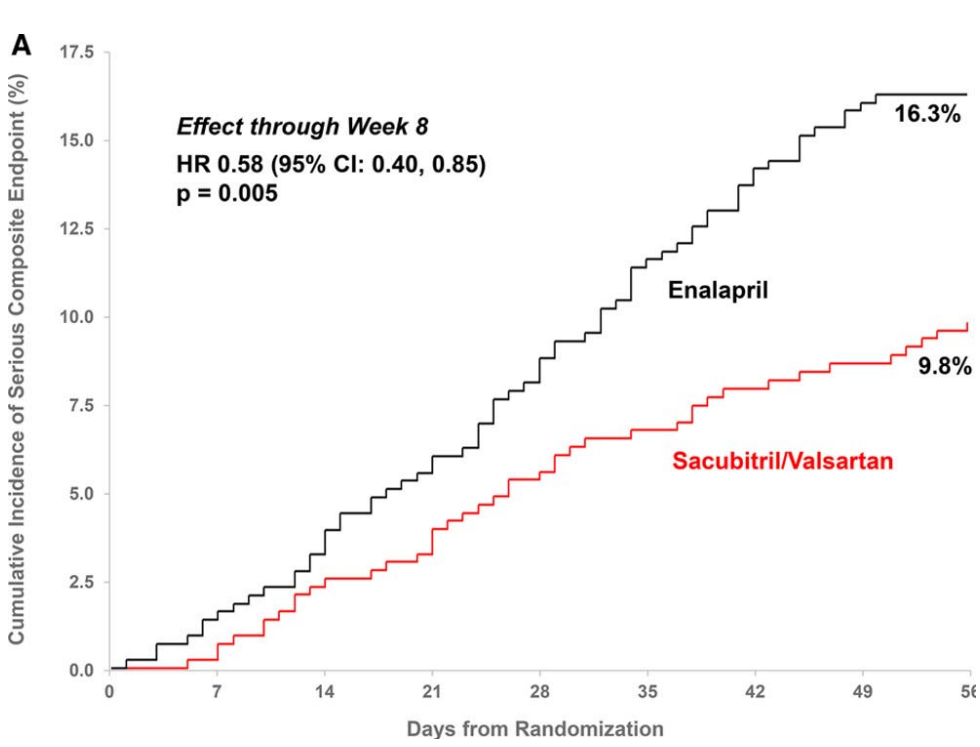
Abraham et al. JACC Heart Failure. 2018 Oct;6(10):874-883

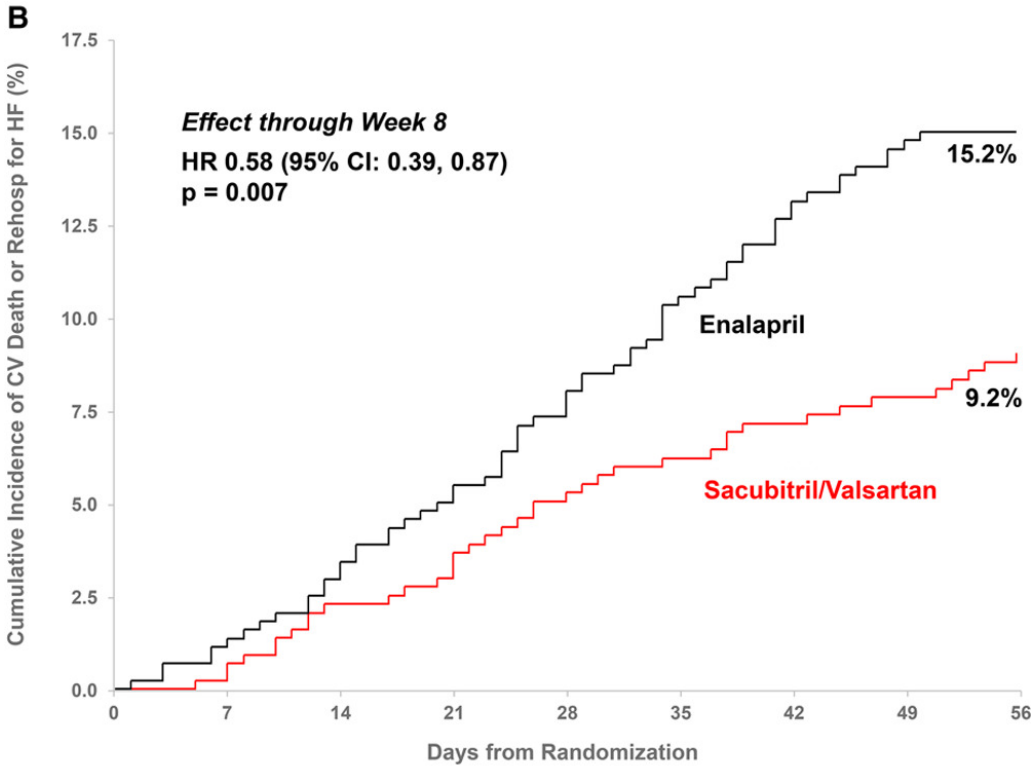
Clinical Trials: Pioneer HF Trial



Velazquez et al, NEJM 2019; 380:539-548

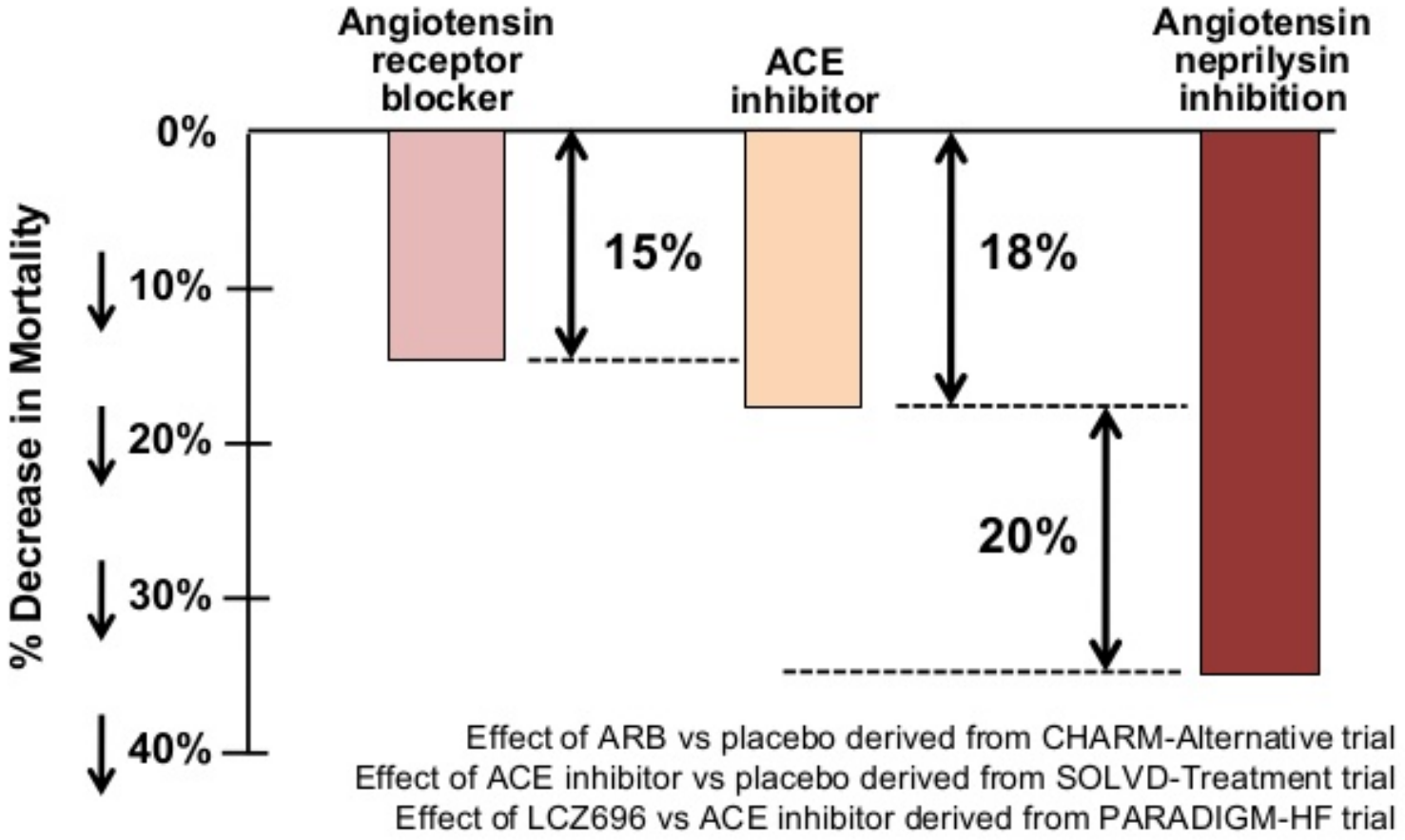
Clinical Trials: Pioneer HF Trial





Morow et al, Circulation. 2019;139:2285–2288

Sacubitril/valsartan Mortality



McMurray et al. NEJM 2014. 371(11):993-1004

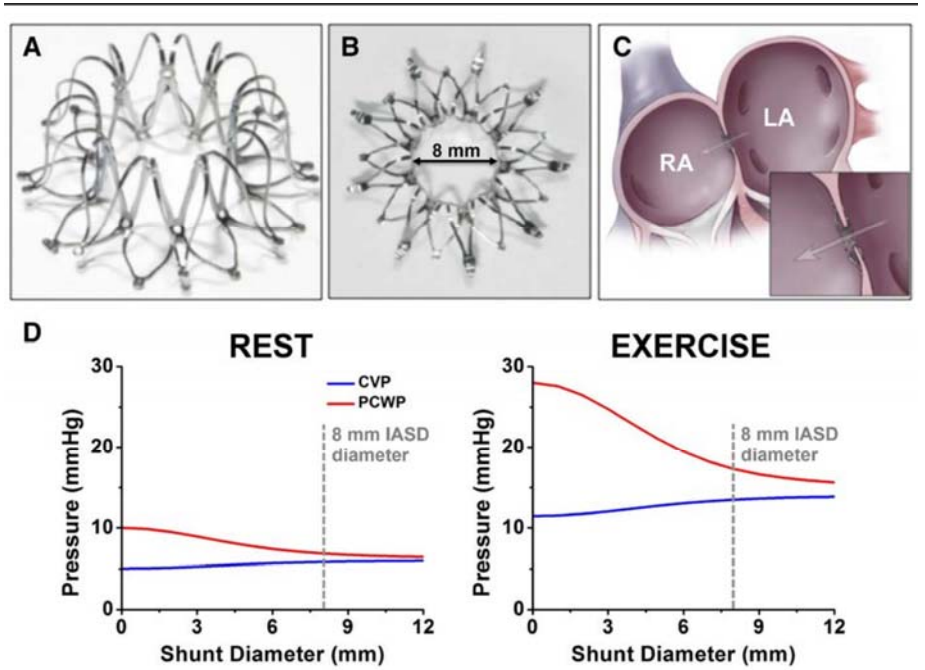
Clinical Trials: Reduce LAP HF

Interatrial Device in HFpEF

Randomized sham-controlled trial.

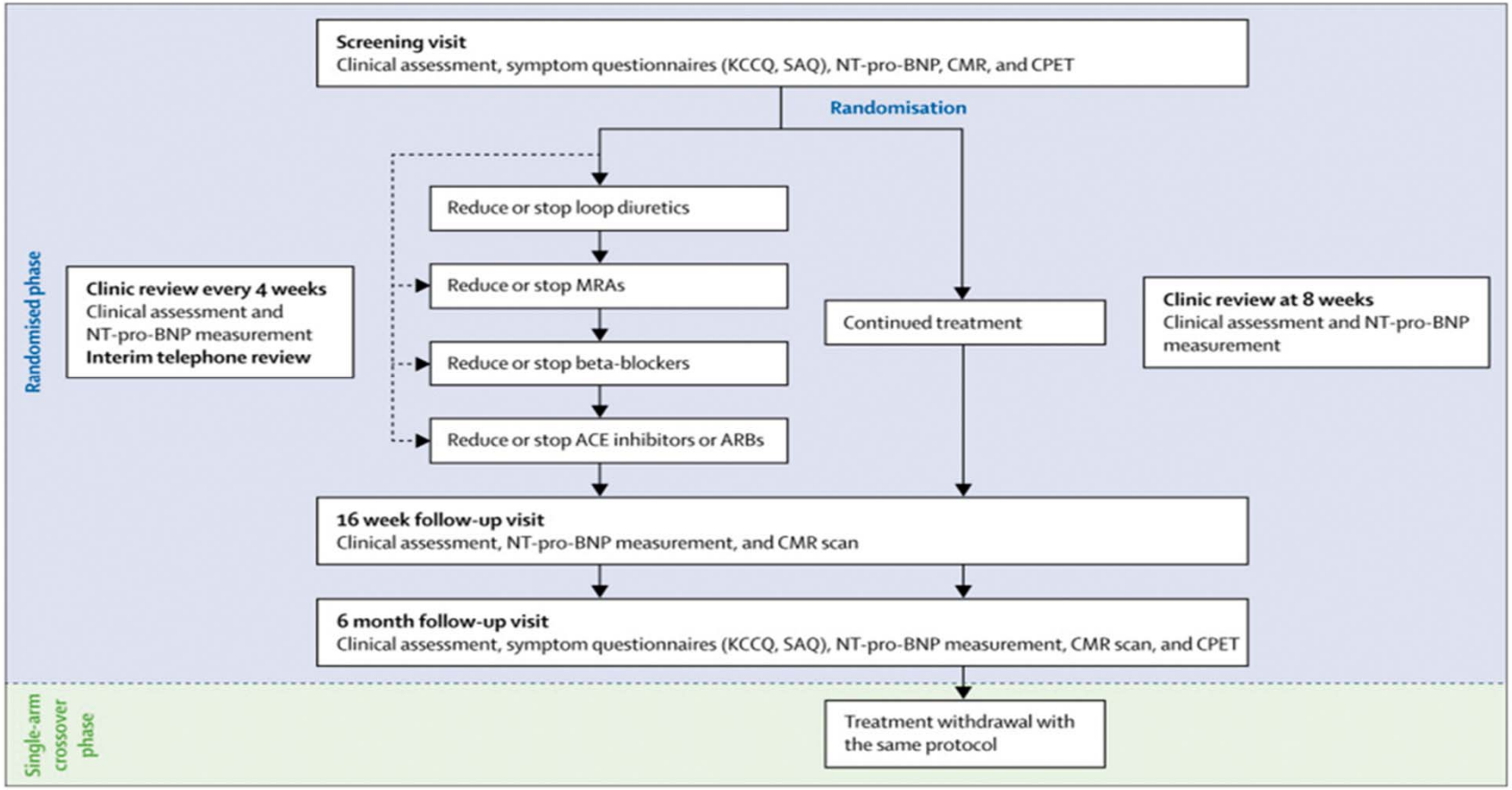
In 44 patients with HF and EF ≥40%.

Unloads the left atrium and reduces pulmonary capillary wedge pressure during exercise.



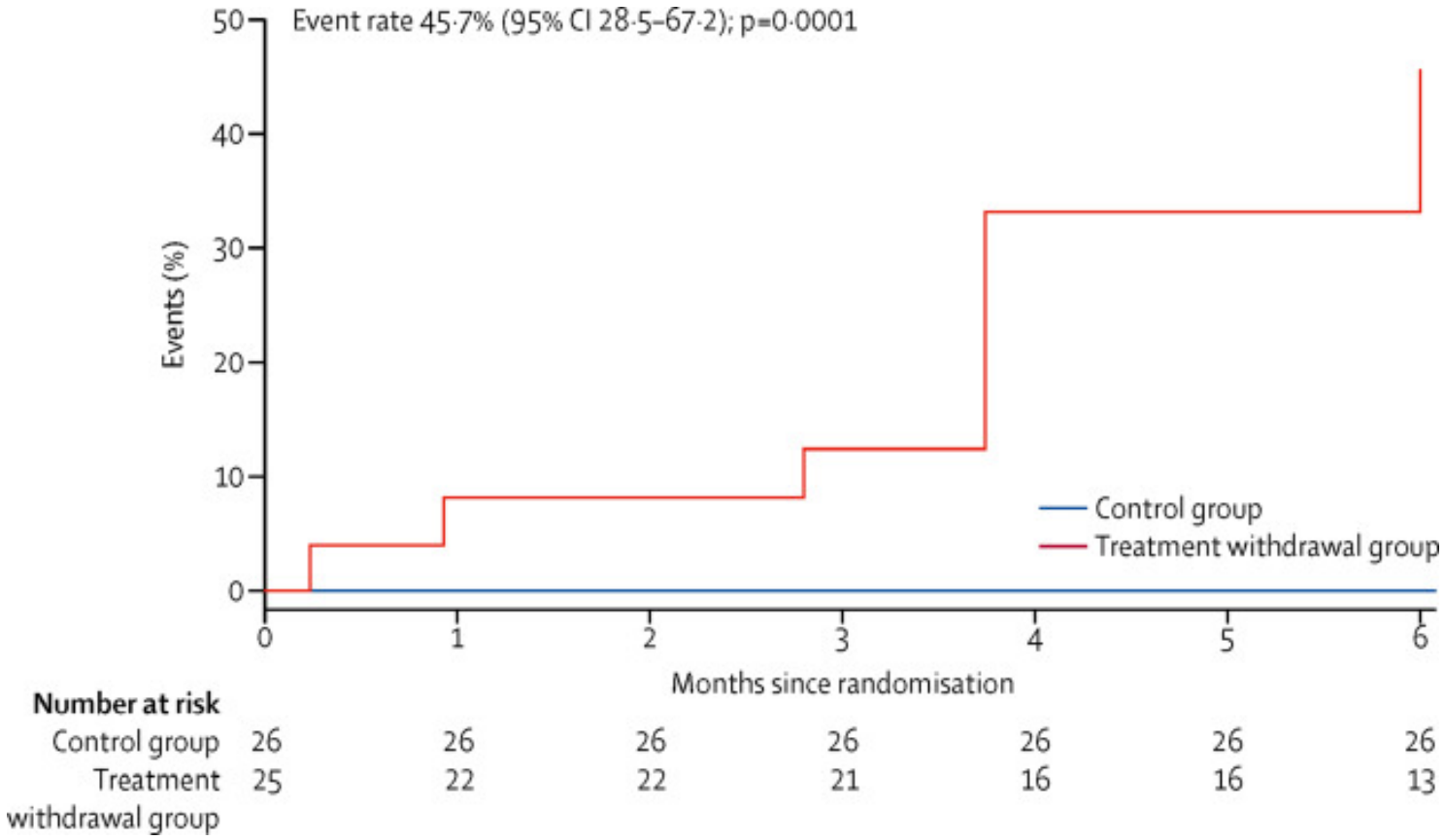
Felman et al. Circulation. 2018;137:364–375

Clinical Trials: TREAD HF Trial



Halliday et al. Lancet January 2019, 61-73

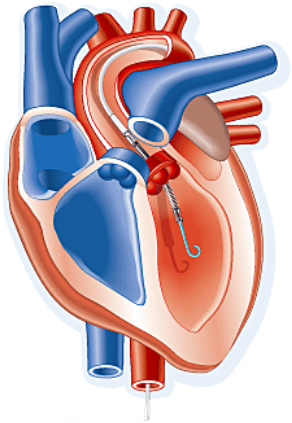
Clinical Trials: TREAD HF Trial



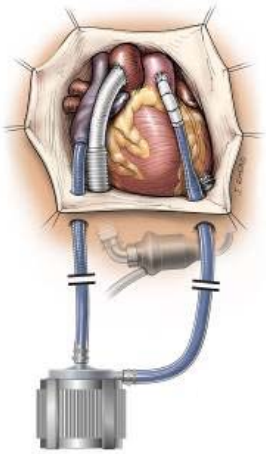
Halliday et al. Lancet January 2019, 61-73

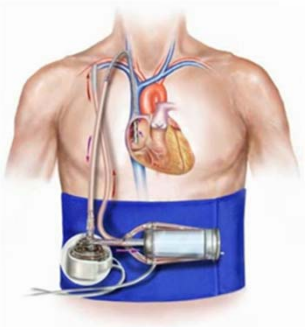
Duration of Support

Percutaneous



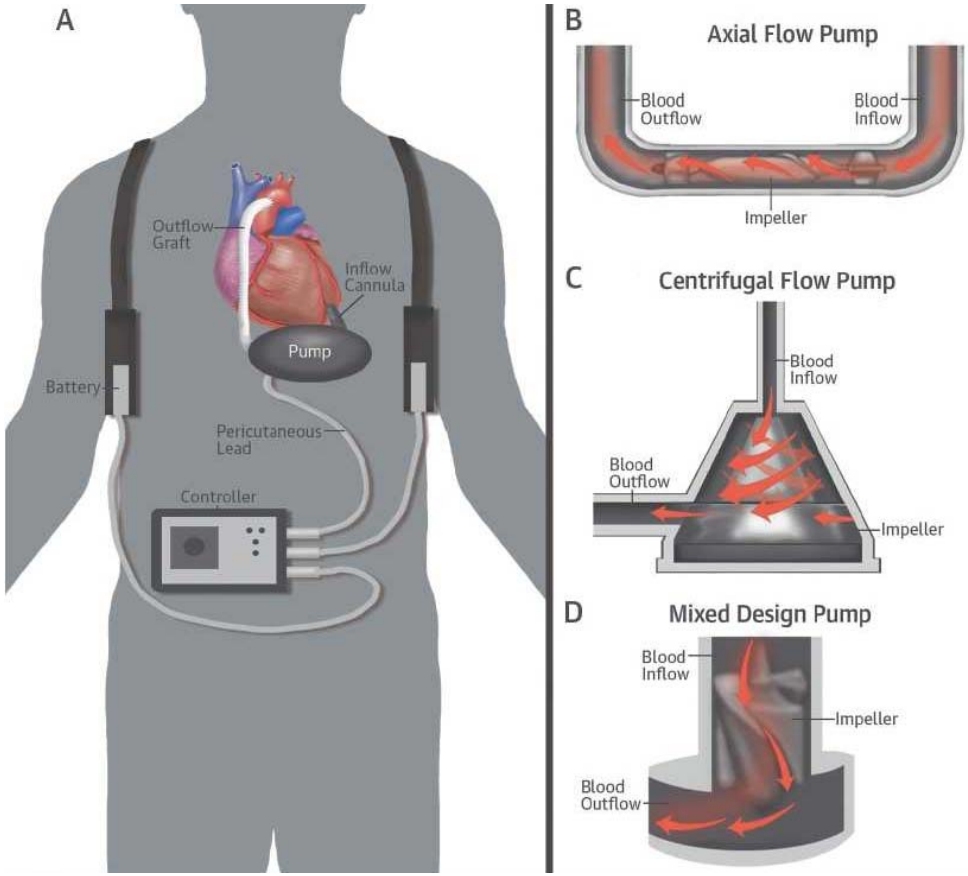
Paracorporal





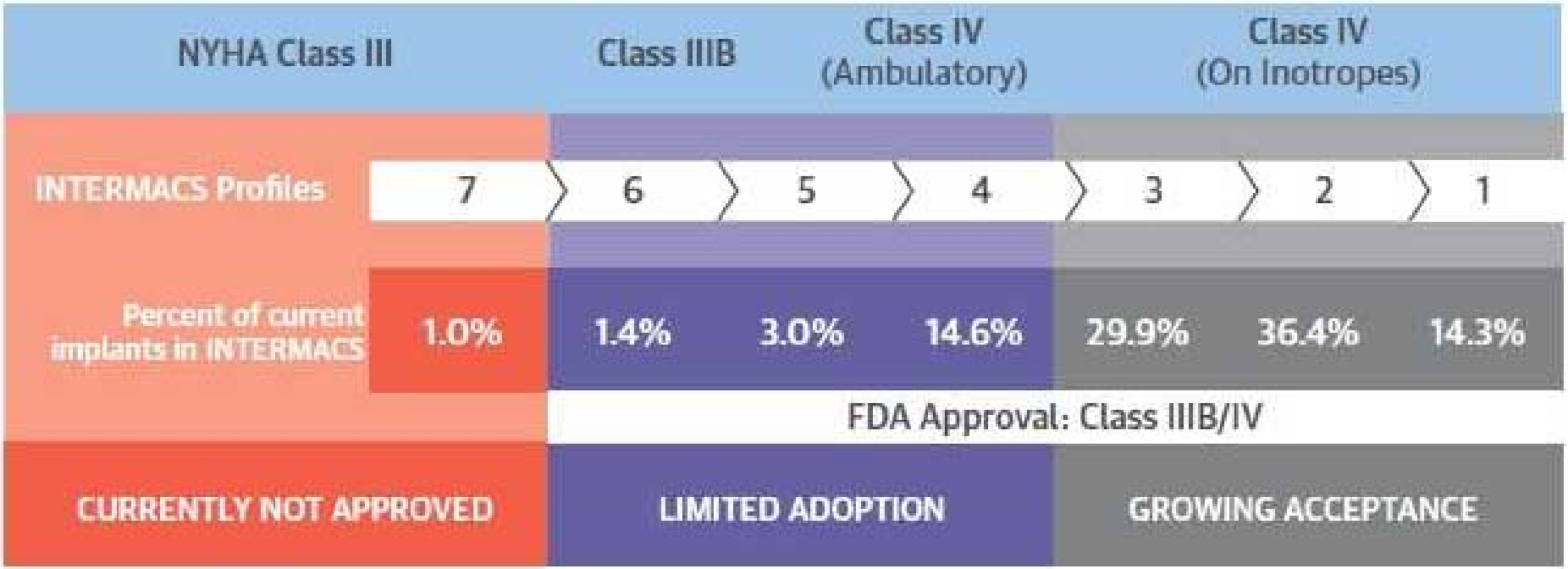
Implanted

Types of Continuous Flow Devices



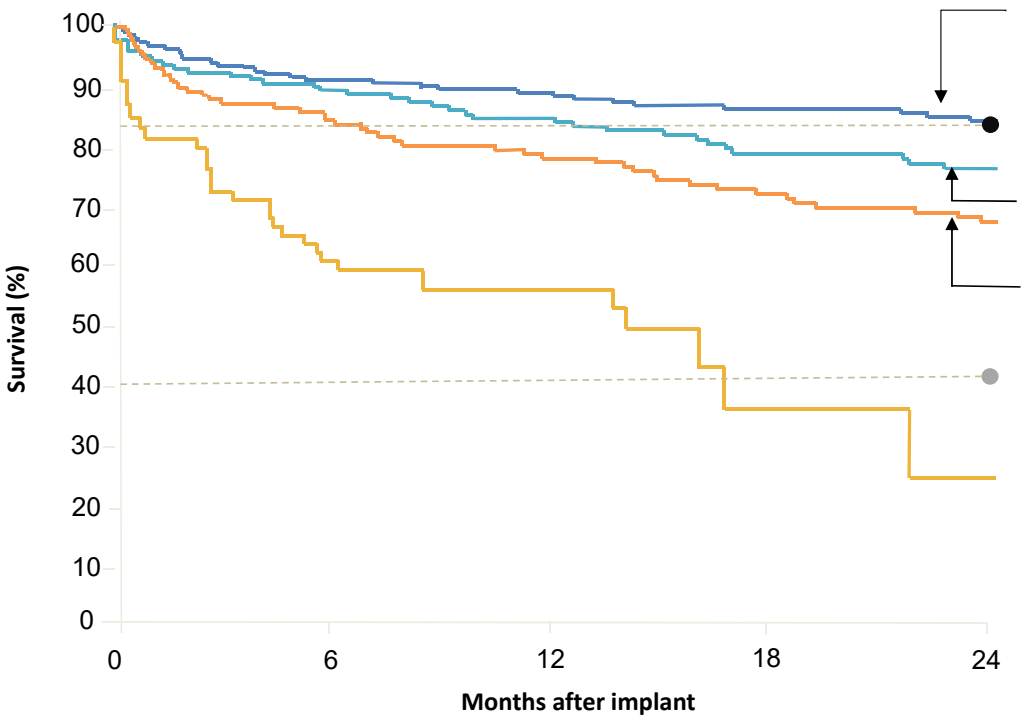
Mancini, JACC. 2015;65(23):2542-2555

Use of LVADs and Disease Severity



Mancini et al. JACC. 2015;65(23):2542-2555

LVAD Survival



HeartMate 3 LVAD (2018)[2]
83%

Heart Transplant[1*]
82%

HeartMate II™ LVAD (2018)[2]
76%

HeartMate II LVAD (2017)[3]
68%

OMM (2017)[4]
41%

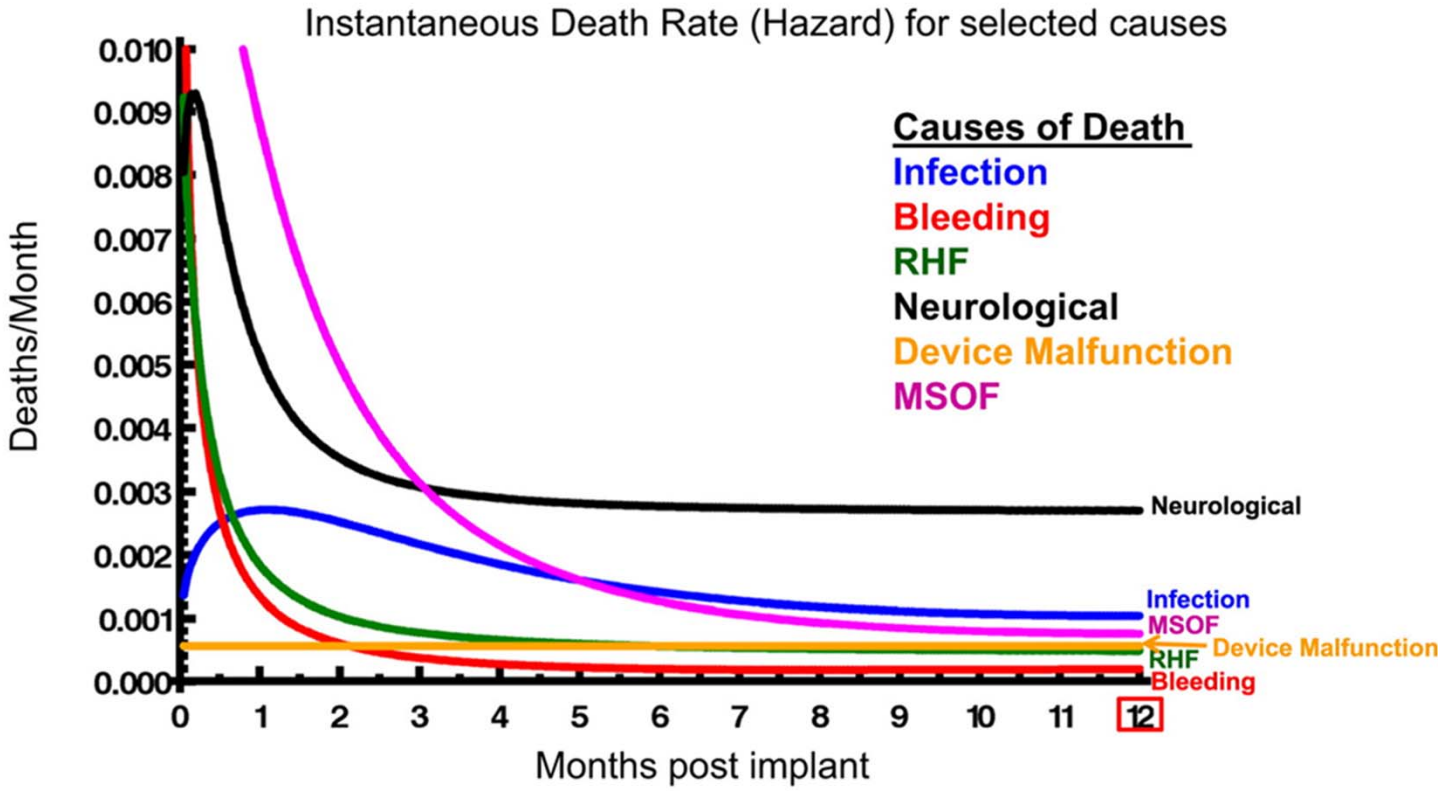
HeartMate™ XVE (2009)[5]
24%

*82% 2-year survival for heart transplant patients between 2009 and 2015.[2]

References: 1. Lund LF, Khush KK, Cherikh WS, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-fourth Adult Heart Transplantation Report—2017; Focus theme: allograft ischemic time. *J Heart Lung Transplant*. 2017;36:1037-1046. **2.** Mehra MR, Goldstein DJ, Uriel N, et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med*. 2018;378(15):1386-1395. **3.** Rogers JG, Pagani FD, Tatooles AJ, et al. Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure. *N Engl J Med*. 2017;376:451-60. **4.** Starling RC, Estep JD, Horstmanshof DA, et al. Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: The ROADMAP Study 2-Year Results. *J Am Coll Cardiol HF*. 2017;5:518-527. **5.** Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009;361:2241-2251.

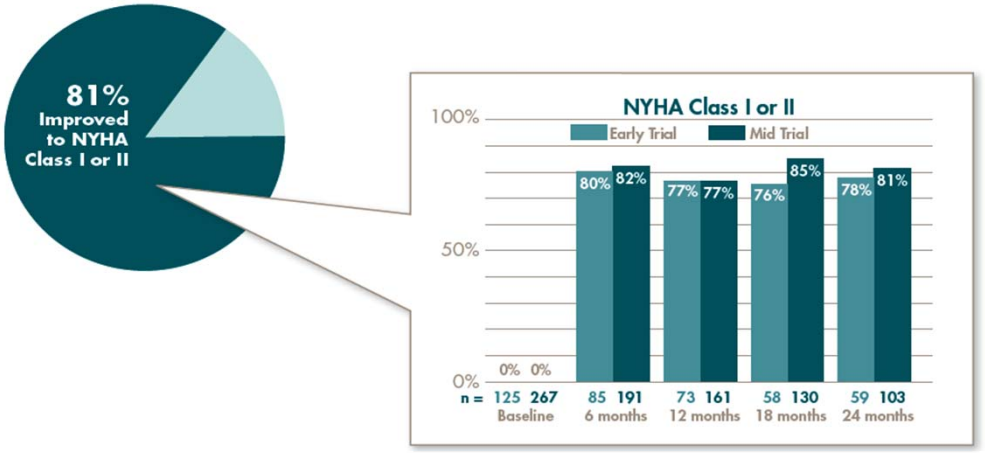
LVAD complications

Intermacs **Continuous Flow LVAD/BiVAD Implants: 2008 – 2013, n = 9372**

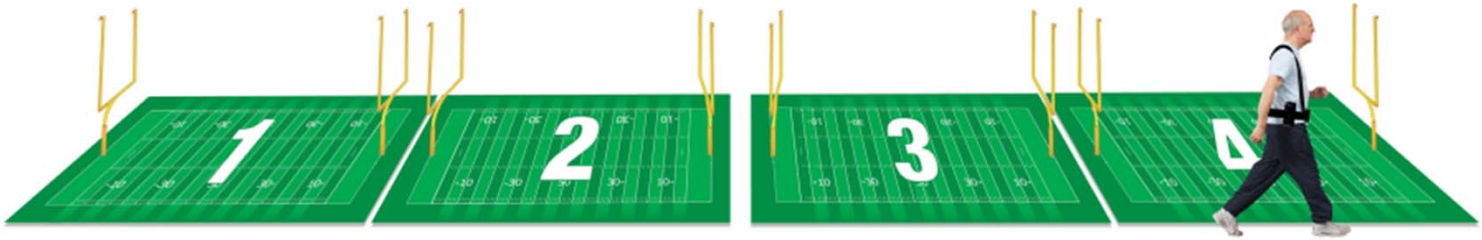


Intermacs JHLT 2014;33, 555–564

Quality of life with LVAD



- 100% of HeartMate II DT patients were NYHA Class IIIB/IV status at baseline[1]
- 81% of patients improved to NYHA Class I or II by 24 months[1]



At 6 months, patients are able to walk 377 yards – *the length of almost 4 football fields* – in 6 minutes

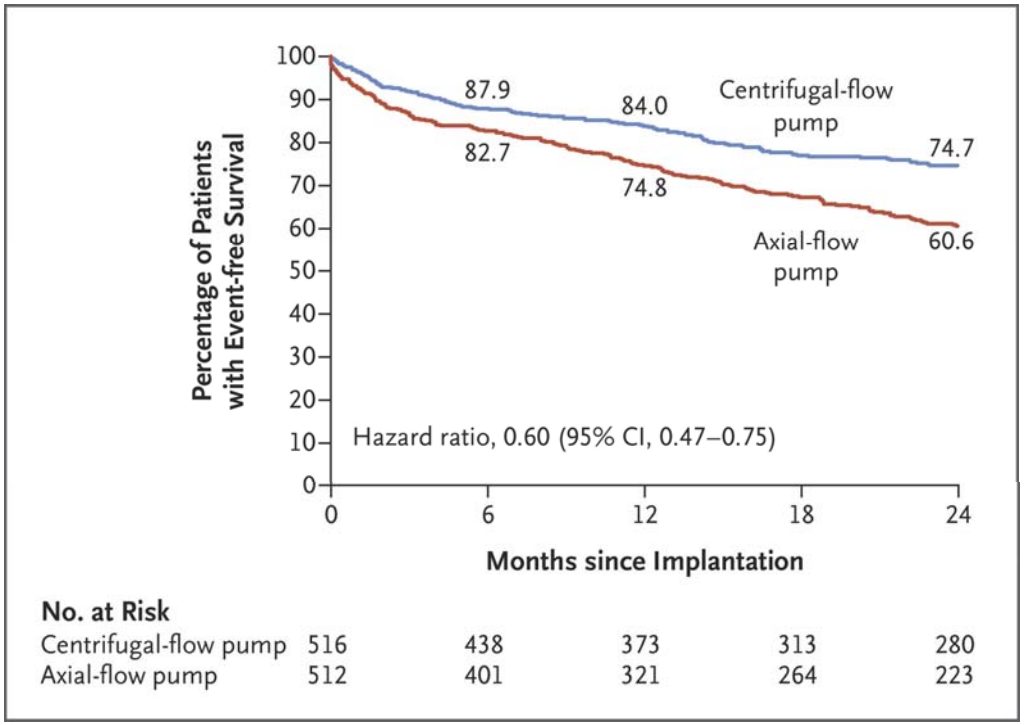
Circ Heart Fail. 2012;5(2):241-248.
Ann Thorac Surg 2011;92:1406 –13.

Clinical Trial: Heart Mate 3

- Randomized non inferiority and superiority trial.
- HM2 vs HM3.
- The composite primary end point was survival at 2 years free of disabling stroke or survival free of reoperation to replace or remove a malfunctioning device.

Mehra et al. NEJM 2019; 380:1618-1627

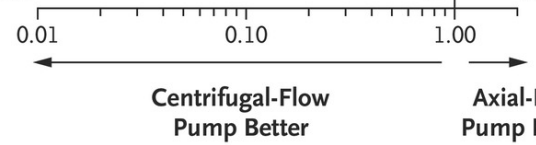
Clinical Trials: Heart Mate 3



Mehra et al. NEJM 2019 380:1618-1627

Clinical Trials: Heart Mate 3

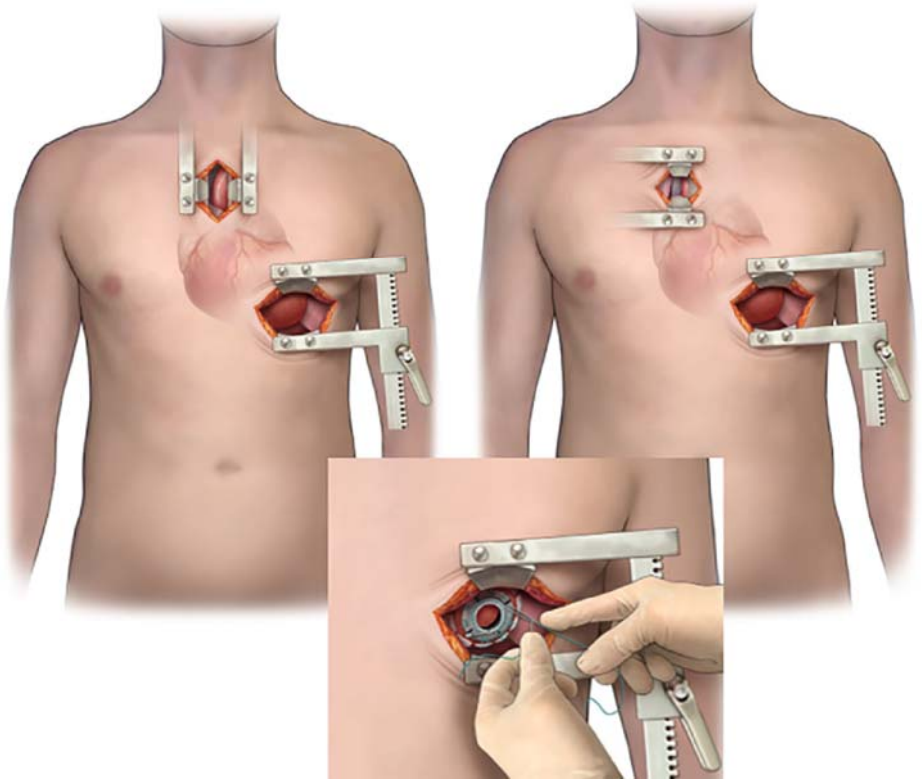
Adverse Event	Centrifugal-Flow Pump	Axial-Flow Pump	Centrifugal-Flow Pump	Axial-Flow Pump	Relative Risk (95% CI)	P Value
	no. of patients with events (%)		*events per patient-yr*			
Suspected or confirmed pump thrombosis	7 (1.4)	70 (13.9)	0.01	0.12	0.08 (0.04–0.16)	<0.001
Any stroke	51 (9.9)	98 (19.4)	0.08	0.18	0.42 (0.30–0.57)	<0.001
Disabling stroke	26 (5.0)	38 (7.5)	0.04	0.07	0.54 (0.34–0.85)	0.008
Any bleeding	225 (43.7)	278 (55.0)	0.61	0.95	0.64 (0.57–0.72)	<0.001
Gastrointestinal bleeding	126 (24.5)	156 (30.9)	0.31	0.49	0.64 (0.54–0.75)	<0.001
Other neurologic event	59 (11.5)	47 (9.3)	0.09	0.08	1.25 (0.88–1.79)	0.21
Any major infection	300 (58.3)	285 (56.4)	0.82	0.82	1.00 (0.89–1.12)	0.96
Right heart failure	176 (34.2)	143 (28.3)	0.27	0.23	1.15 (0.94–1.42)	0.18
Cardiac arrhythmia	185 (35.9)	207 (41.0)	0.37	0.45	0.82 (0.70–0.97)	0.02
Respiratory failure	111 (21.6)	98 (19.4)	0.19	0.17	1.10 (0.86–1.40)	0.44
Renal dysfunction	73 (14.2)	56 (11.1)	0.11	0.08	1.36 (0.98–1.89)	0.07
Hepatic dysfunction	25 (4.9)	27 (5.3)	0.03	0.04	0.78 (0.46–1.34)	0.38



Mehra et al. NEJM 2019 380:1618-1627

Clinical Trials: Lateral Trial

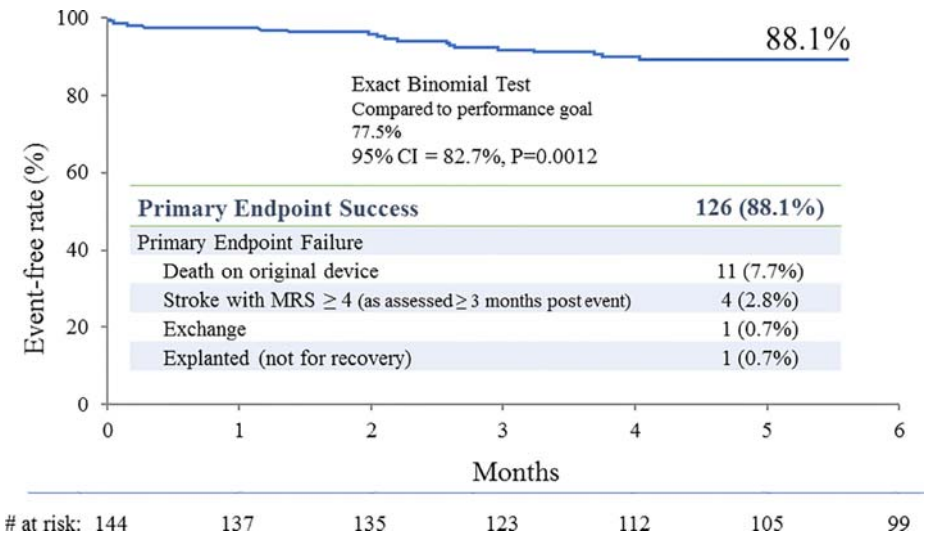
Lateral Thoracotomy in 144 patients
Heart Ware device

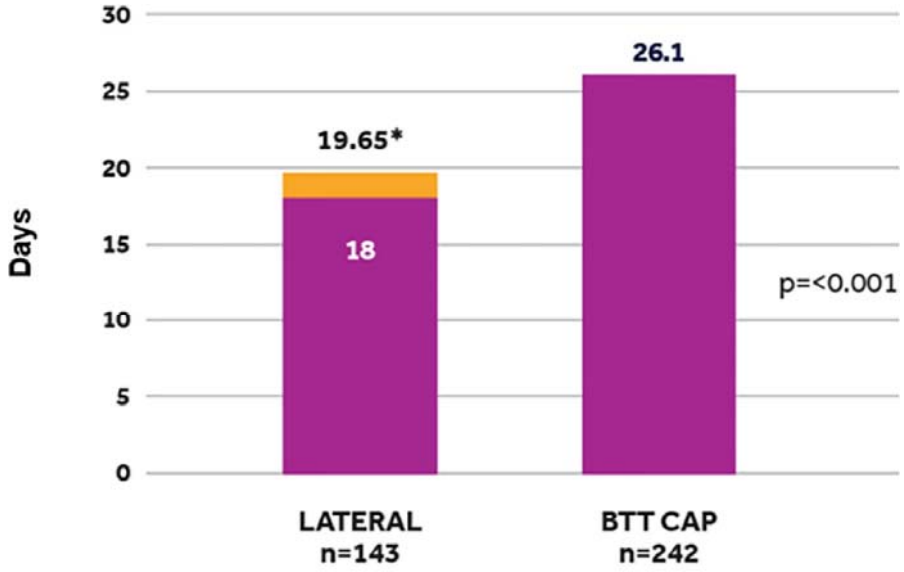


McGee et al. JHLT 2019 Apr;38(4):344-351

Clinical Trials: Lateral Trial

Lateral Thoracotomy in 144 patients
Heart Ware device



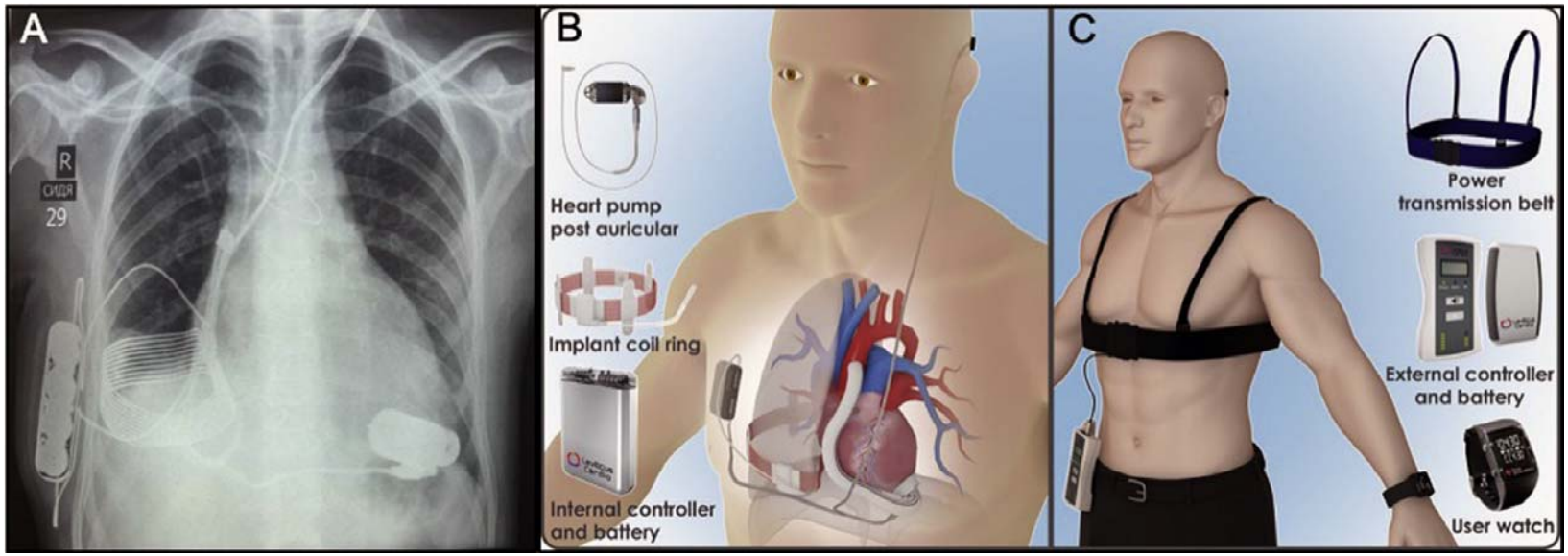


*Upper Boundary of 95% Confidence Interval

McGee et al. JHLT 2019 Apr;38(4):344-351

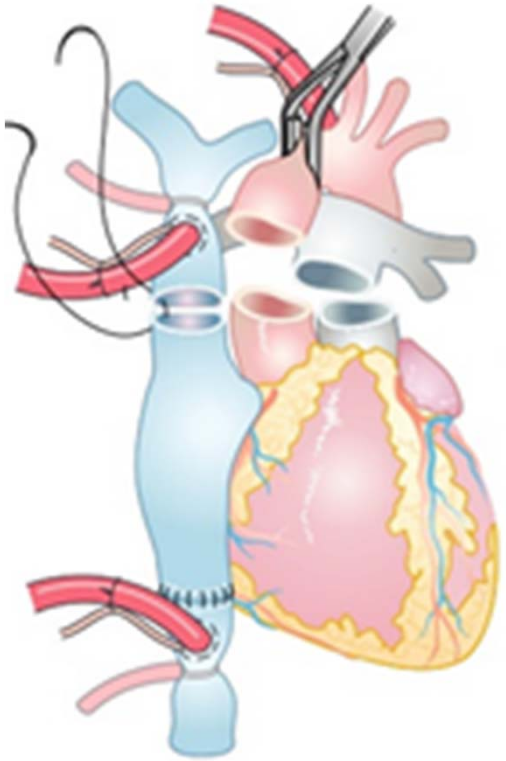
Clinical Trials: FIVAD

Fully Implanted Ventricular Assist Device
A Jarvik 2000 pump, powered wirelessly using both internal and external components designed by Leviticus Cardi.
Allows patients to walk without any physical impediments for up to 8 hours.

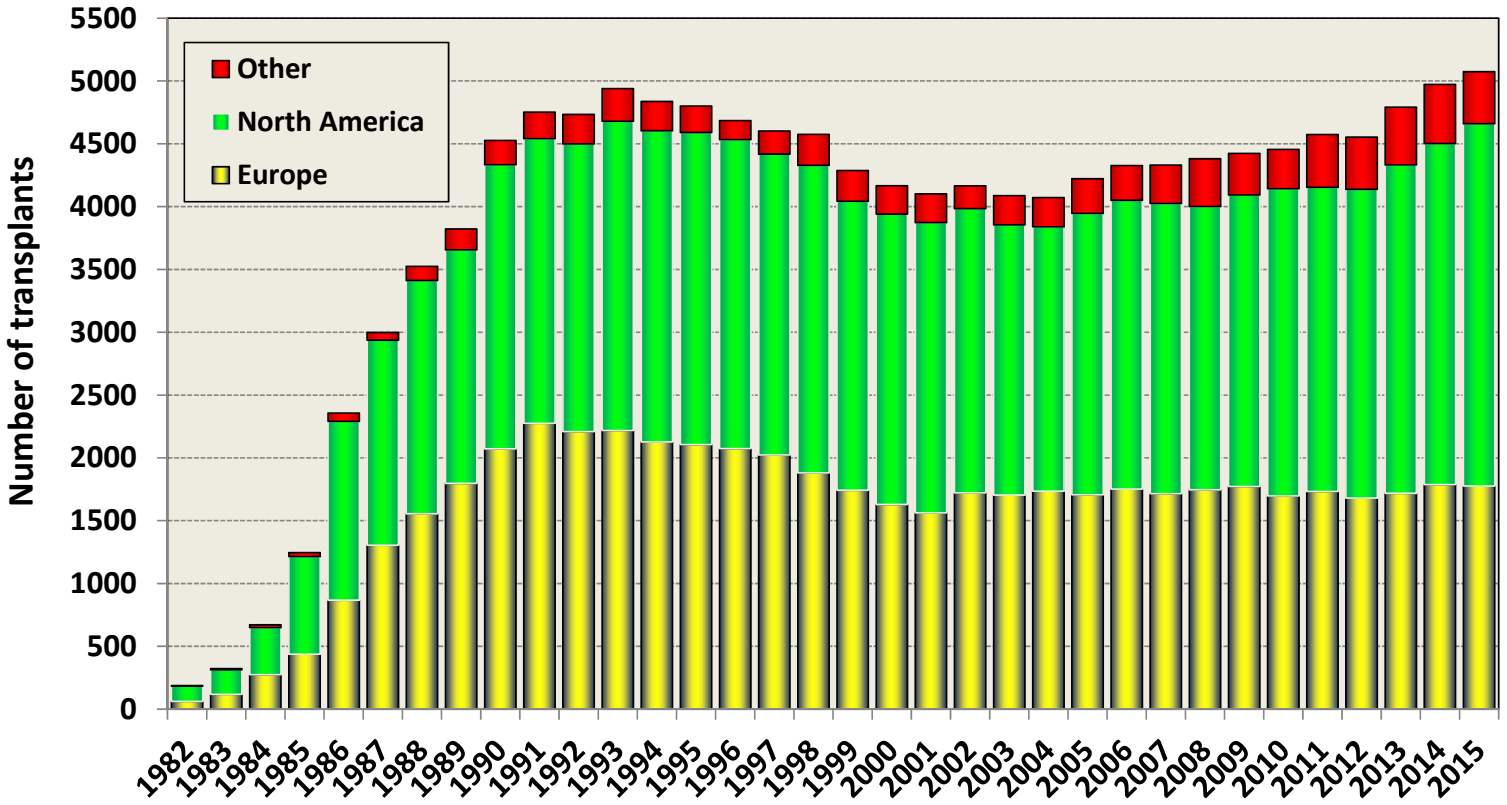


Pya et al. JHTL 2019; 38(4): 339–343

Heart Transplant



Heart Transplants by Year



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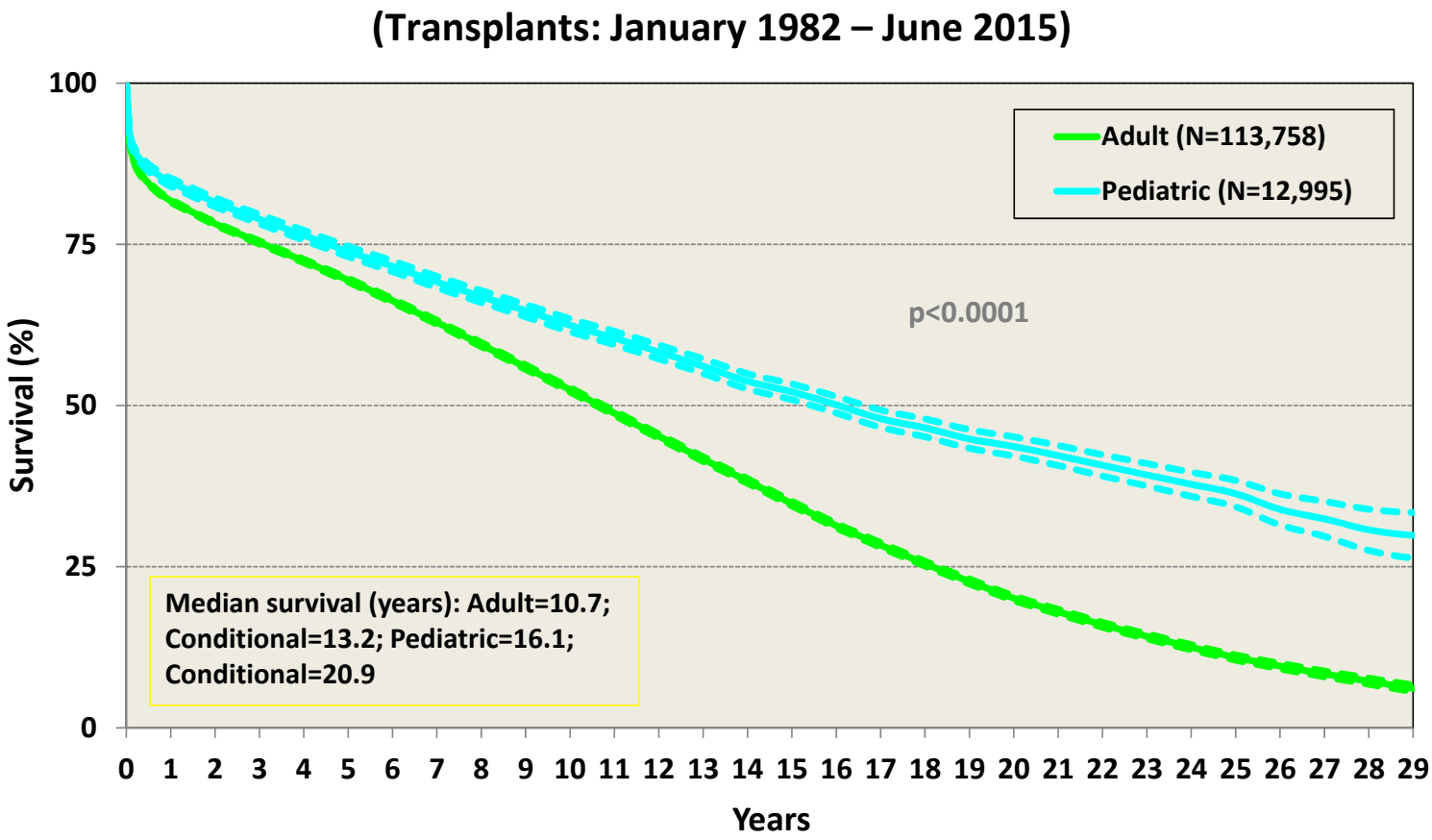
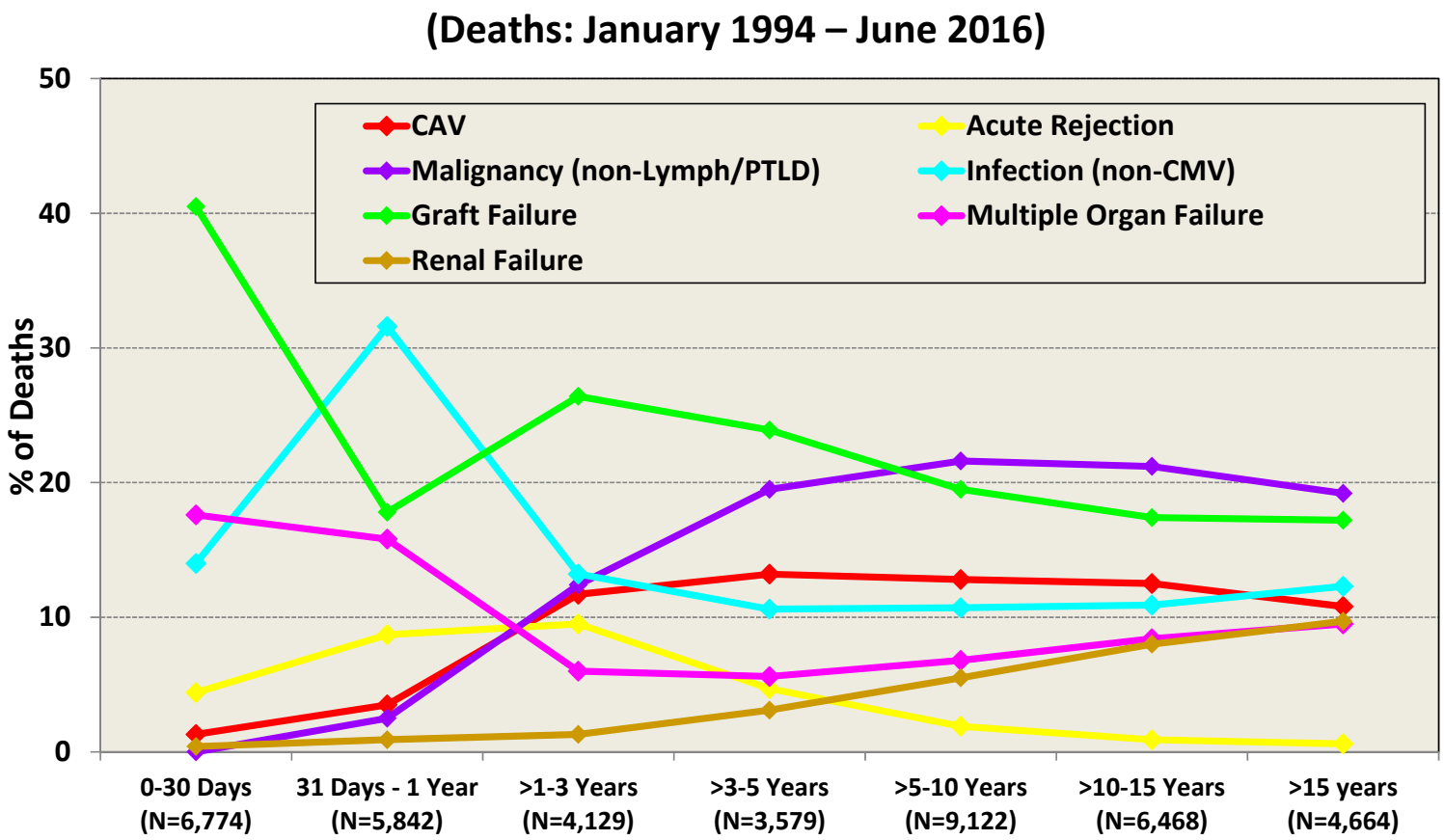
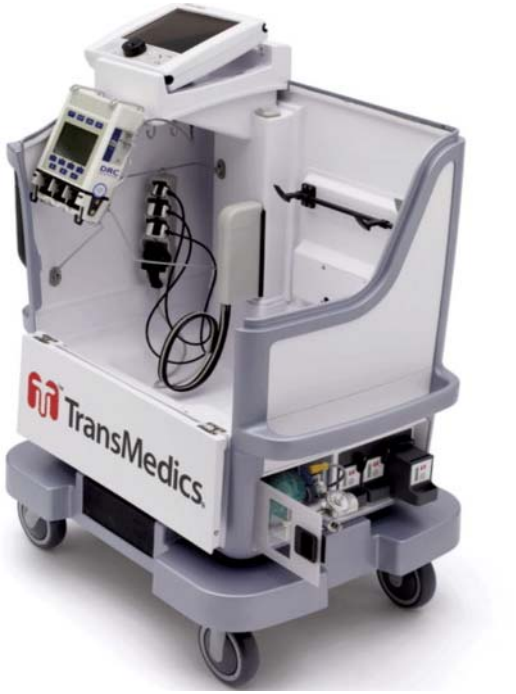
Survival by Age Group

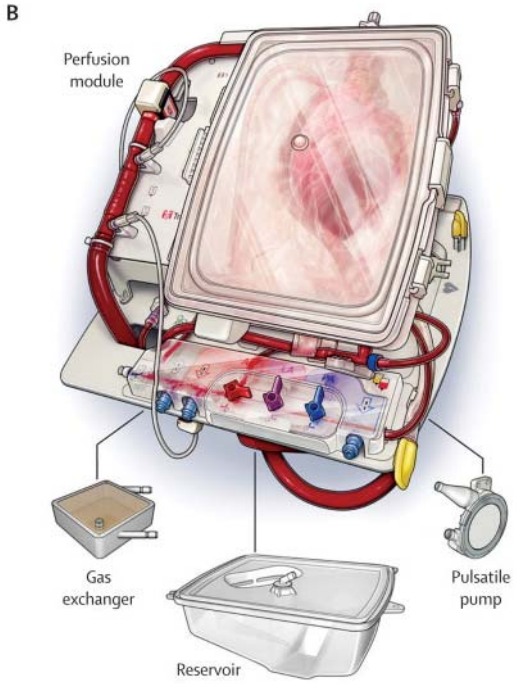


Leading Causes of Death



Organ Preservation

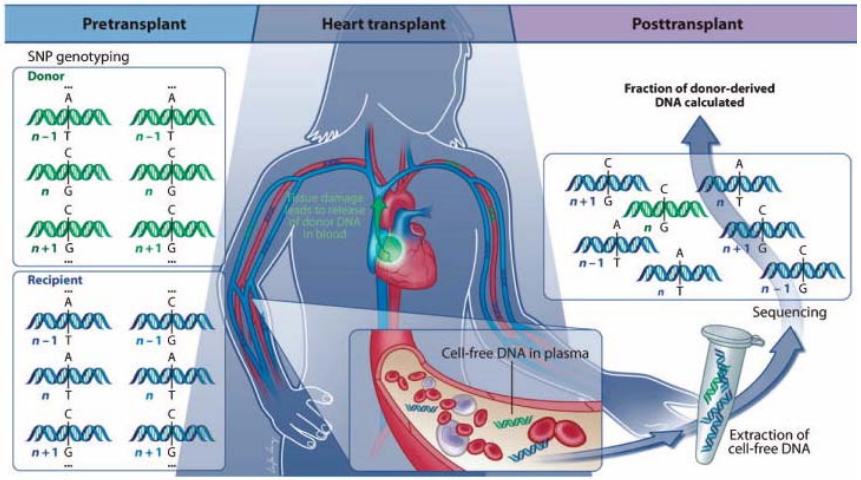




Ardehali et al. Lancet 2015 June;385(9987):2577–84

Cell free DNA

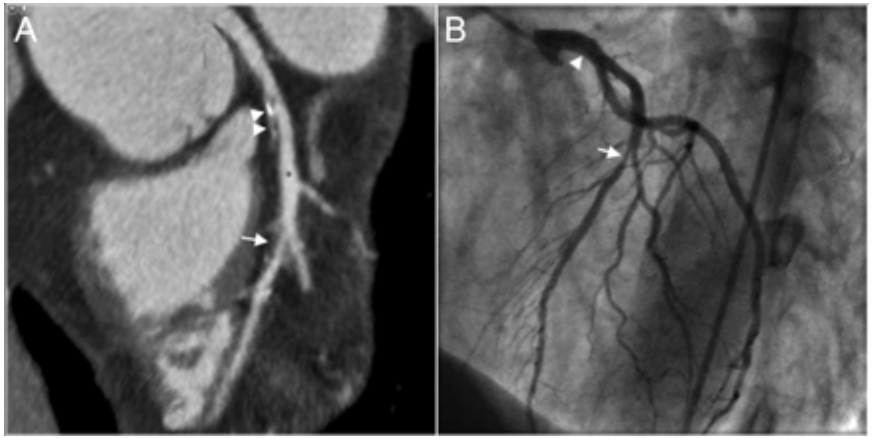
- Detection of increasing amounts of the donor's DNA in the blood of the recipient.
- The donor DNA accounted for less than 1% of all cell-free DNA in the recipient's blood.
- During rejection episodes, the donor DNA increased to 4%.



De Vlaminck, et al. Sci Transl Med. 2014 Jun 18;6(241):241

Transplant vasculopathy

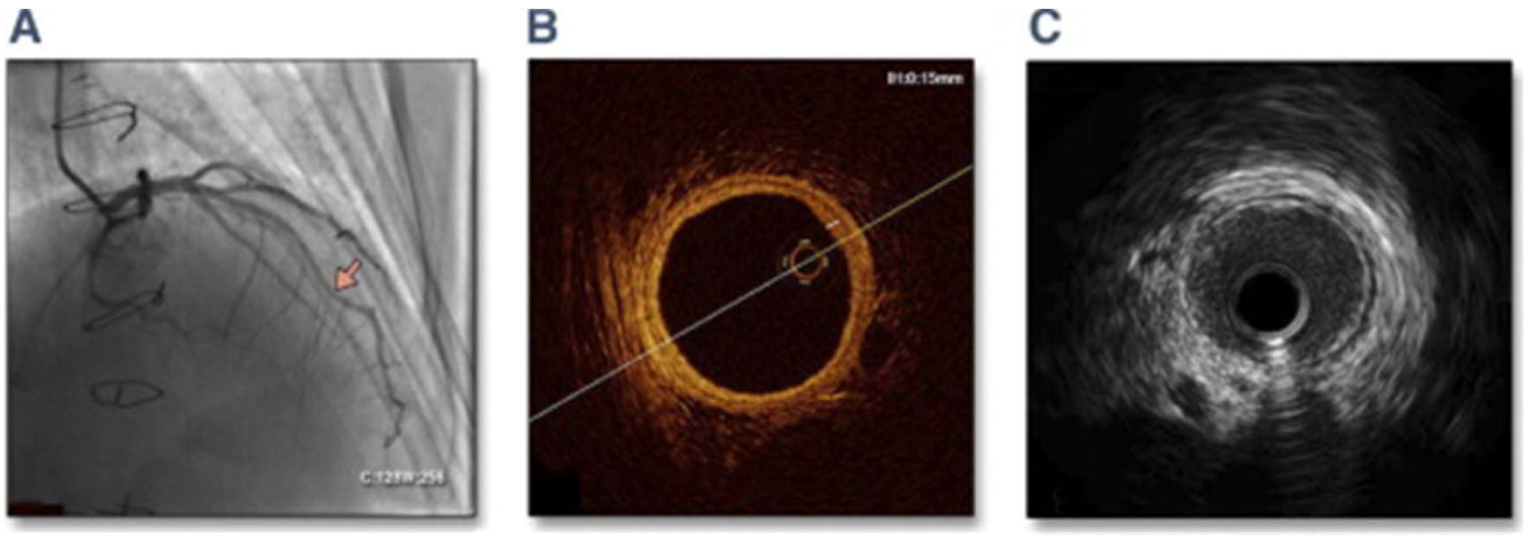
- DSE has a sensitivity of 80% and specificity of 88%.
- SPECT has a sensitivity of 21% to 92% and specificity of 55% to 100%.
- CTA has a sensitivity of 94% and specificity of 92%.



Teuterberg et al. JHLT 2015 Feb;34(2):158-60

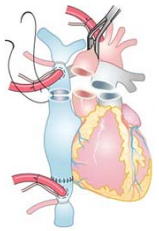
Transplant vasculopathy

Optical coherence tomography (OCT), allows greater resolution of the coronary vasculature and plaque characterization than IVUS and it is the new gold standard.

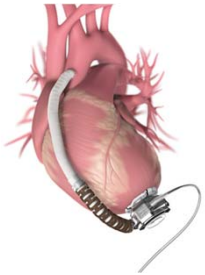


Hoe et al. JACC Img. 2012;5(6):662-663.
Teuterberg et al. JHLT 2015 Feb;34(2):158-60

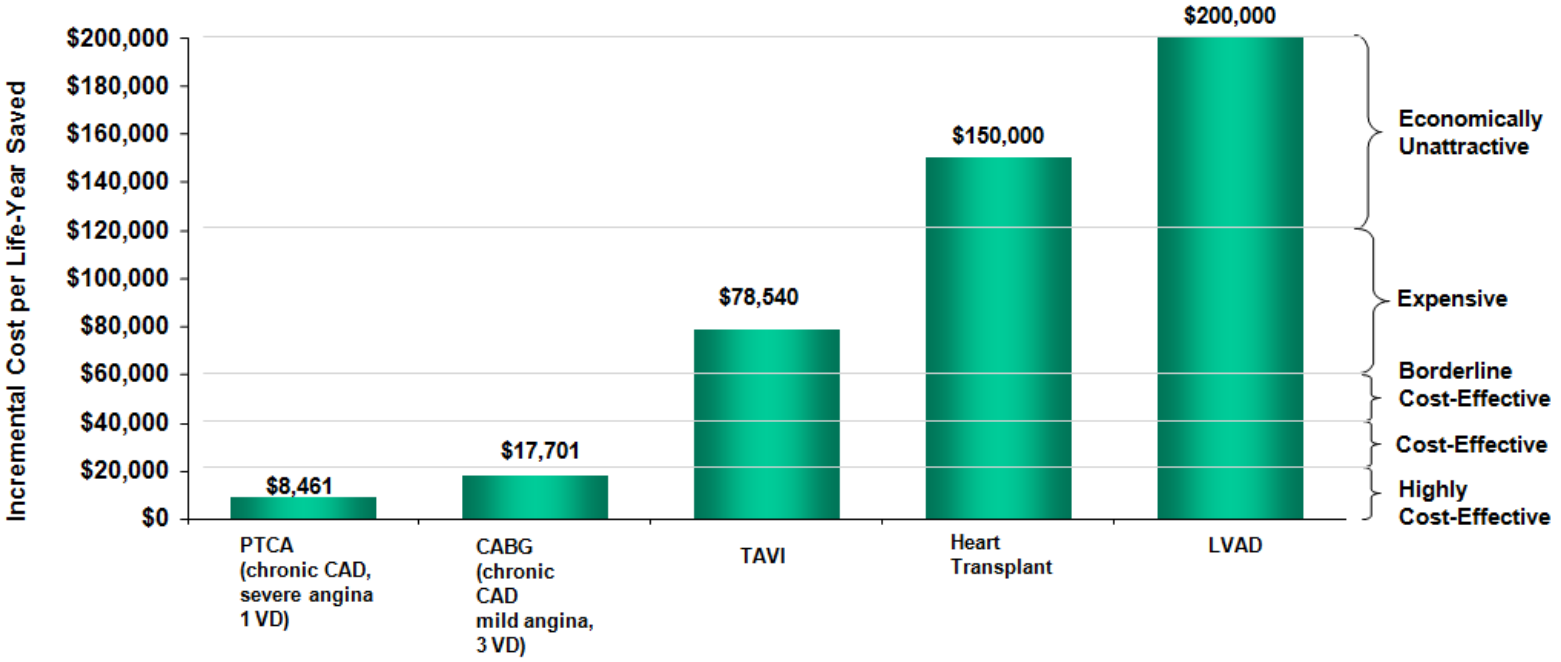
Heart Transplant and LVADs



Transplant	LVAD
150K	200K
Waiting time 3K	Unlimited supply
Infection Renal Failure	Infection Thrombosis
Malignancy	No Malignancy



Costs comparisons



Roberts PR. European Heart Journal. 2001;21:712-719.

Mark DB. www.theheart.org. ACC News. April 12, 2011.

What to do for HFrEF?

Quadruple therapy:
ARNI
Beta Blocker
MRA
SGLT2 inhibitor

Cumulative risk reduction in all-cause mortality, 74% relative, 26% absolute.
NNT 4 in just 2 years
Increase in health status, decrease in hospitalizations

Dr. Greg Fonarow, via Tweeter, Sept 19, 2019

When to Refer

I IV inotropes

N NYHA IIIB/IV or persistently elevated natriuretic peptides
E End-organ dysfunction
E Ejection fraction ≤35%
D Defibrillator shocks

H Hospitalizations >1
E Edema despite escalating diuretics
L Low BP, high heart rate
P Prognostic medication –progressive intolerance or down-titration of GDMT

Yancy et al. JACC. 2018; 71:201-230

Heart Failure Guidelines

ACC/AHA 2016 Guideline Heart Failure and 2017 Update

- www.acc.org

Heart Failure Society of America Guideline

- www.hfsa.org

International Society of Heart and Lung Heart Transplant

- www.ishlt.org

European Society of Cardiology

- www.escardio.org

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