Advanced Heart Failure
It all starts early- The role or Primary Care

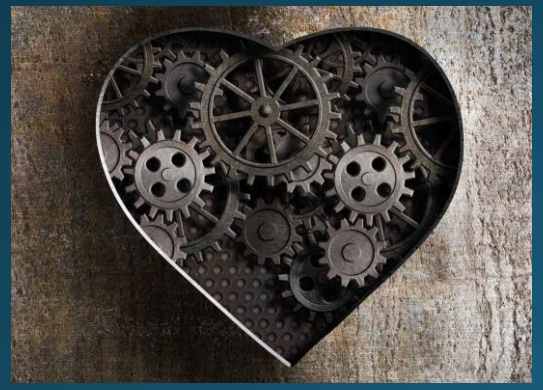
Muhammad Waqas. MD

Medical Director

Advanced Heart Failure, Mechanical Circulatory Support, Heart Transplant &

Pulmonary Hypertension Program

CHI St. Vincent, Heart Clinic Arkansas



CHI St. Vincent

Imagine better health.SM

DISCLOSURES

- NO FINANCIAL DISCLOSURES

Heart failure has devastating public health consequences in the US

Based on data from NHANES 2013 to 2016, an estimated **6.2 million** Americans ≥20 years of age had HF

Projections show that the prevalence of HF will increase **46% from 2012 to 2030**, resulting in >8 million people ≥18 years of age with HF.

Additionally, the total percentage of the population with HF is predicted to increase from **2.42% in 2012 to 2.97% in 2030**

Heart Disease and Stroke Statistics—2020 Update

AMERICAN COLLEGE OF CARDIOLOGY AND AMERICAN HEART ASSOCIATION (ACC/AHA) STAGES[1]

AT RISK FOR HEART FAILURE		HEART FAILURE	
Stage A	**Stage B**	**Stage C**	**Stage D**
At high risk for heart failure but without structural changes or symptoms	Structural heart disease but without signs or symptoms of heart failure	Structural heart disease with prior or current symptoms of heart failure	Refractory heart failure including specialized interventions

Increasing Severity

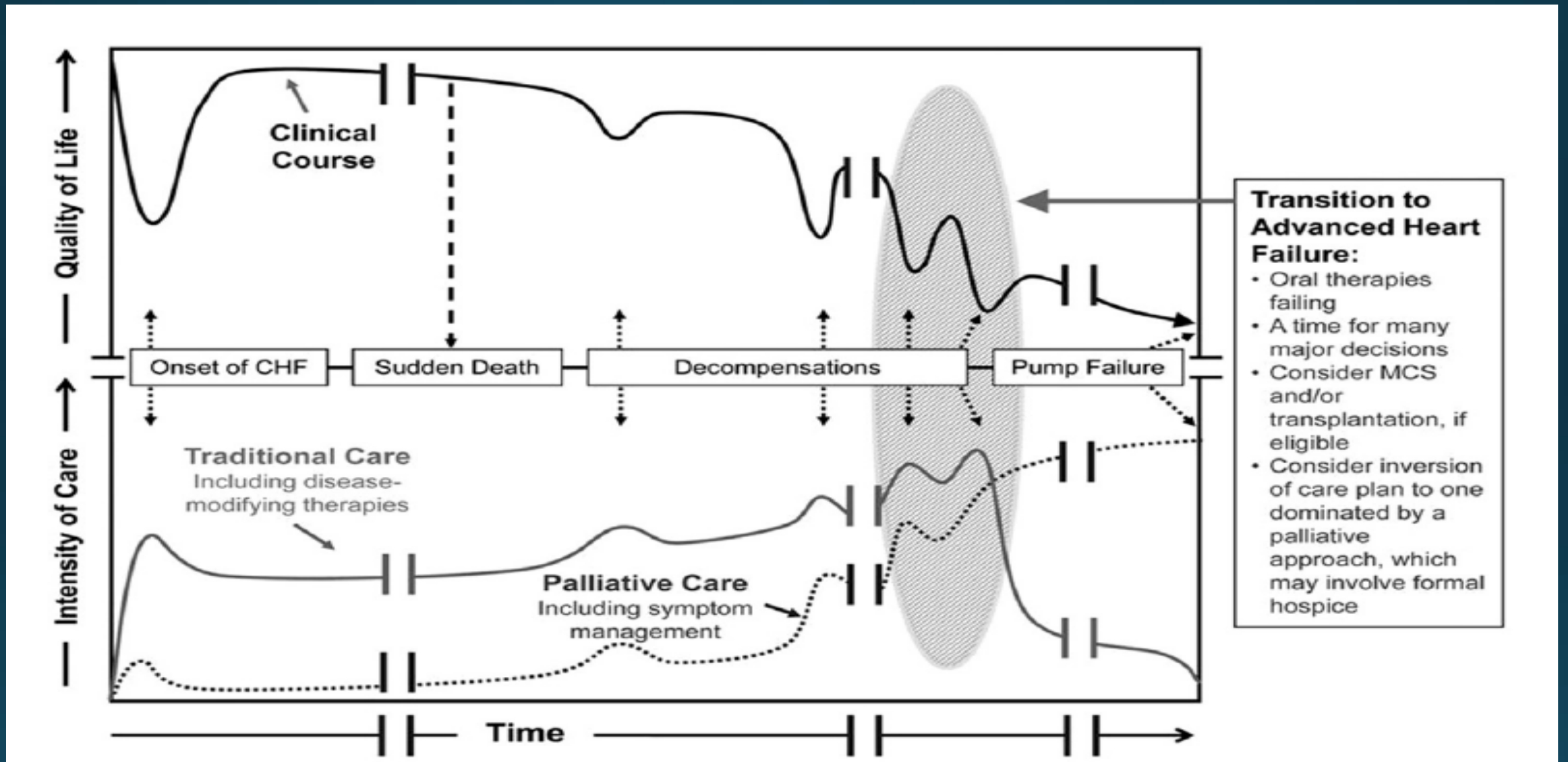
NYHA

Class I
- No limitation in ordinary physical activity

Class II
- Slight limitation during ordinary activity

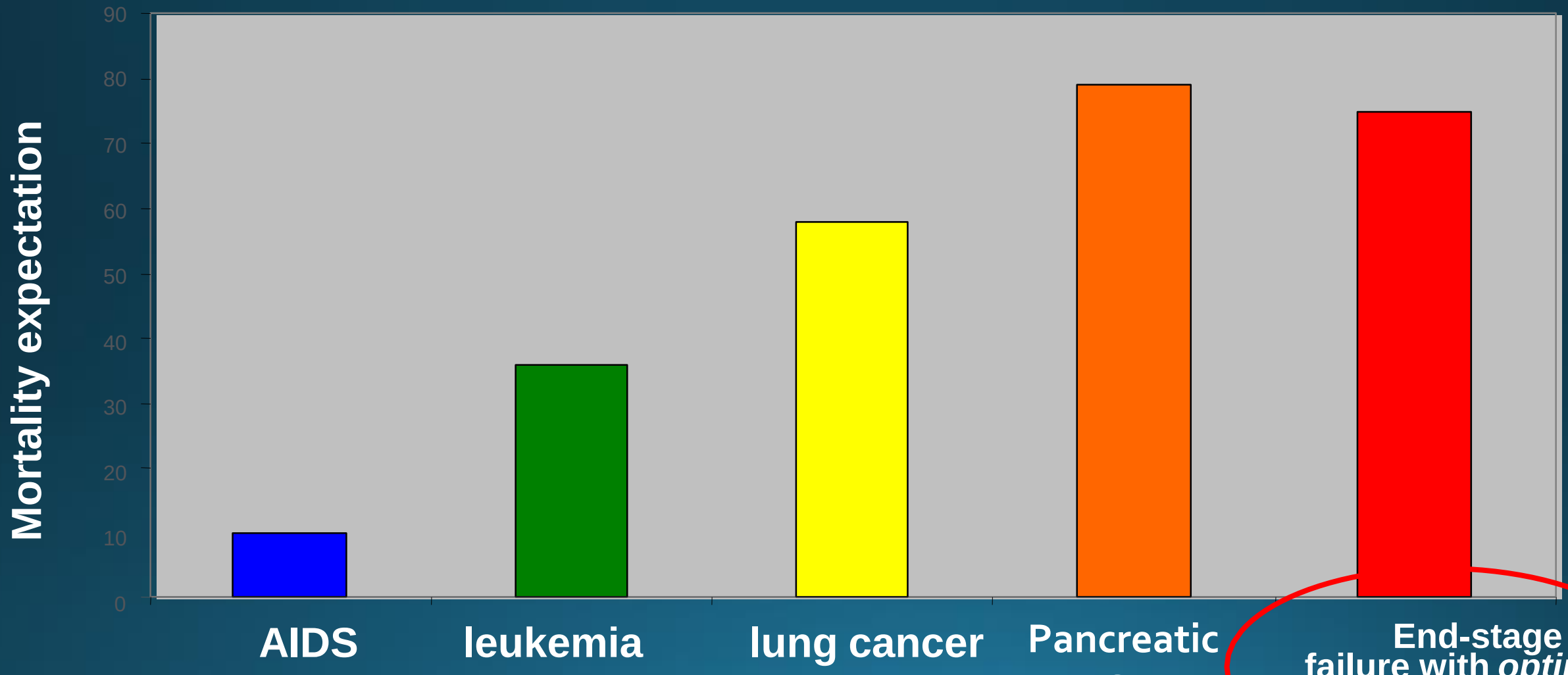
Class III
- **Marked limitation in activity due to symptoms**

Class Iv
- **Severe limitations**
- **Symptoms even while *at rest***



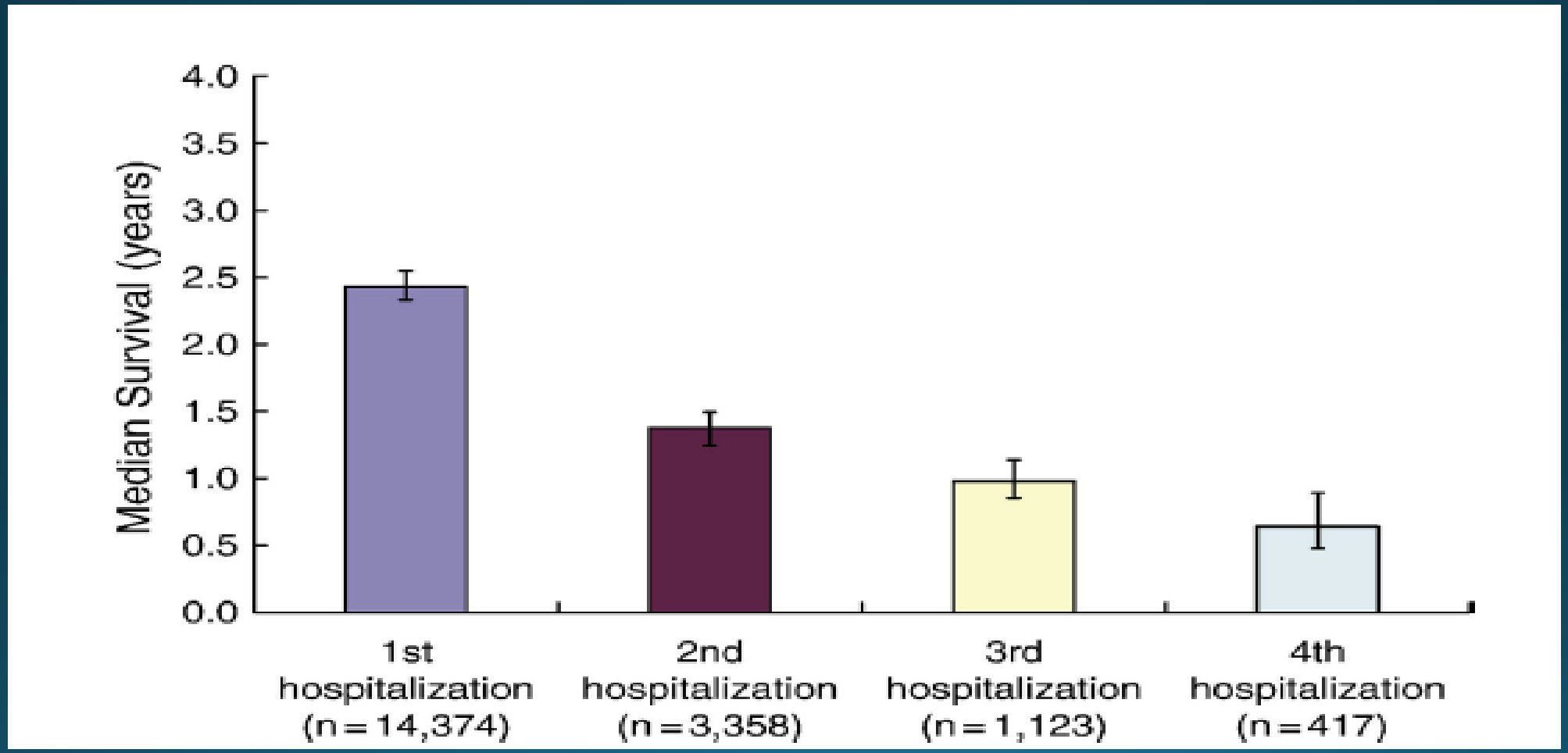
Circulation 2012;125(5):1930.

Advanced Heart Failure Mortality at 1 Year



Lee et al. JAMA 2003 290(19)

Impact of recurrent heart failure hospitalization on mortality



Am Heart J 2007;154

GOALS OF HEART FAILURE MANAGEMENT

- Improve symptoms and quality of life
  - Relieve circulatory congestion
  - Increase tissue perfusion

- Prolong life by slowing disease progression
  - Reduce vasoconstriction
  - Inhibit activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system
  - Inhibit progressive enlargement or remodeling of the left ventricle

Eras of Heart Failure Therapy

PAST | **PRESENT** | **FUTURE**

Edema weight

Exercise Tolerance

Morbidity and mortality

1680 — 1960 — 1990 — 2000 — 20??

Cardiorenal

- Diuretics
- Digitalis

Hemodynamic

- Vasodilator
- Inotropes

Neurohormonal

- ACEI
- BB
- ARBs
- MRA
- HDZ/Nitrates

Biomechanical

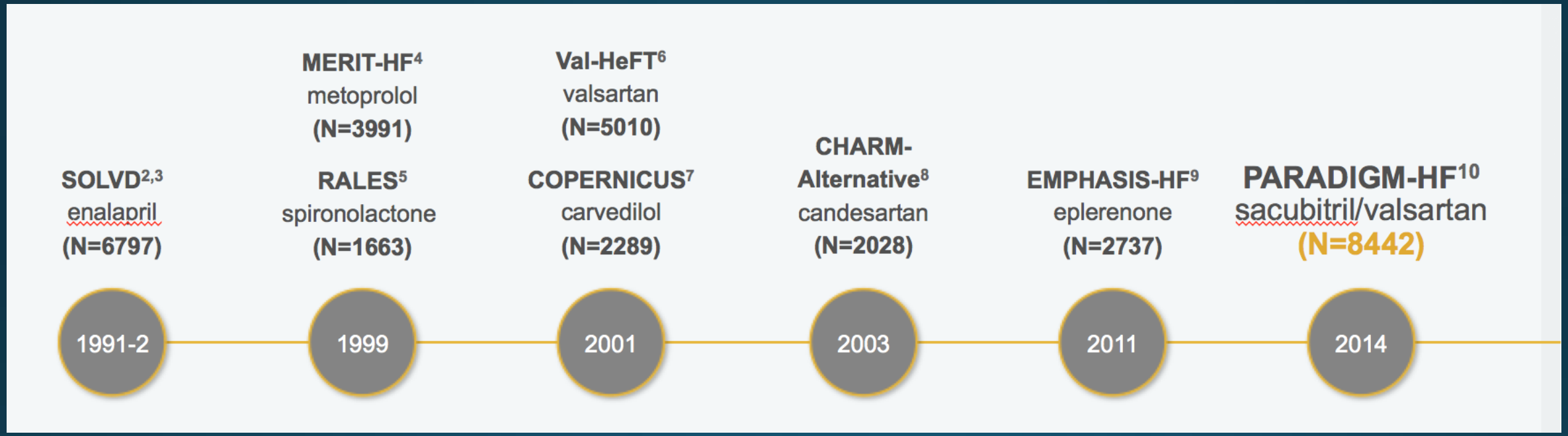
- ICDs
- CRT
- LVAD
- Stem cells

Personalized

- Genomics
- Proteomics
- Epigenetics
- Xenotransplant

Heart Transplant

MEDICAL THERAPY OF HEART FAILURE



MEDICAL THERAPY OF HEART FAILURE

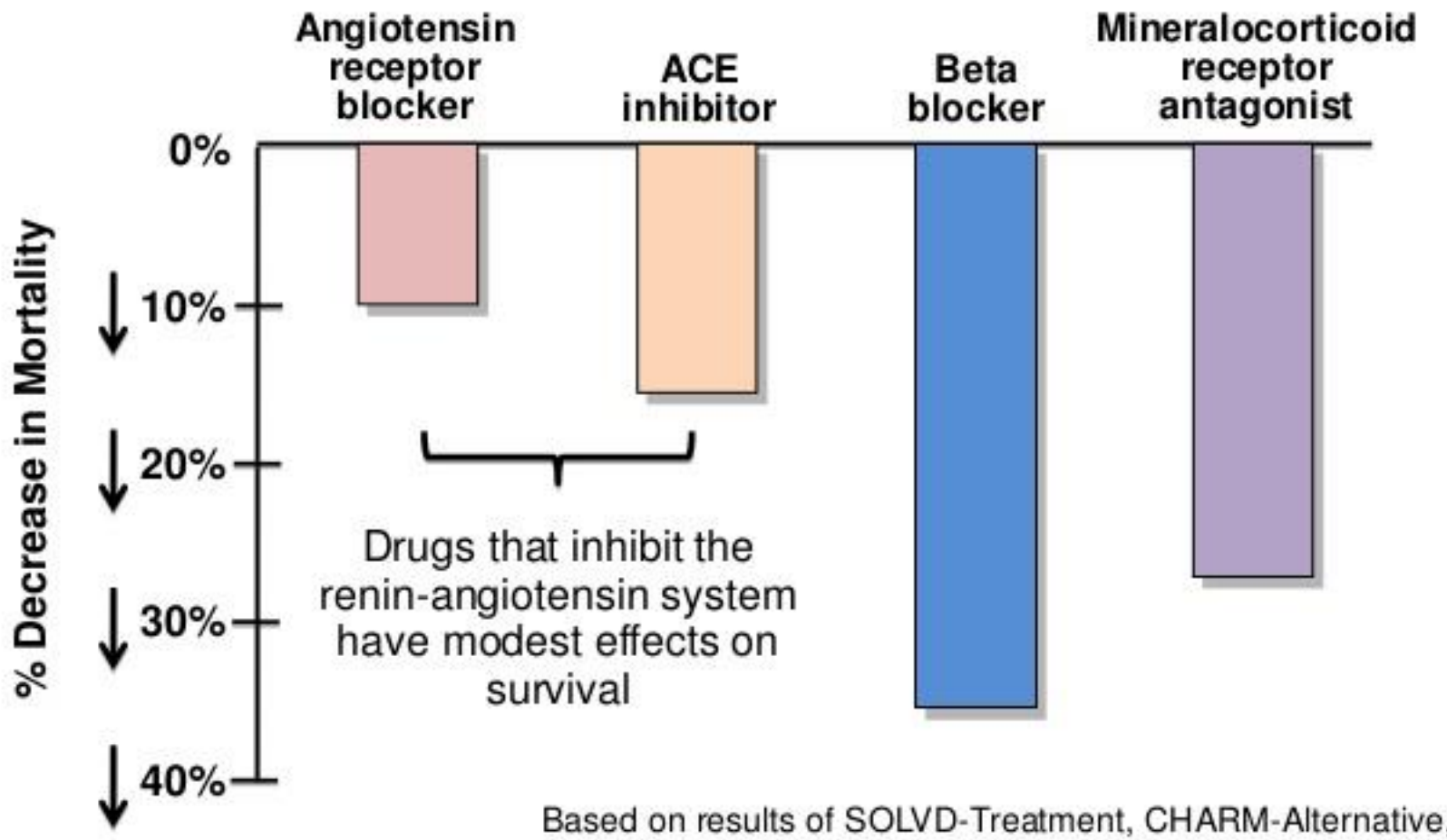
SOLVD[2,3]
enalapril
(N=6797)

1991-2

IGM-HF[10]
l/valsartan
8442)

014

Drugs That Reduce Mortality in Heart Failure With Reduced Ejection Fraction



Based on results of SOLVD-Treatment, CHARM-Alternative, COPERNICUS, MERIT-HF, CIBIS II, RALES and EMPHASIS-HF

MEDICAL THERAPY OF HEART FAILURE Updates

1991-2 — SOLVD[2,3] enalapril (N=6797)

1999 — MERIT-HF[4] metoprolol (N=3991); RALES[5] spironolactone (N=1663)

2001 — Val-HeFT[6] valsartan (N=5010); COPERNICUS[7] carvedilol (N=2289)

2003 — CHARM-Alternative[8] candesartan (N=2028)

2011 — EMPHASIS-HF[9] eplerenone (N=2737)

2014 — PARADIGM-HF[10] sacubitril/valsartan (N=8442)

2019 DAPA-HF

2019

DAPA-HF TRIAL

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

Randomized, parallel group, placebo-controlled trial

AMERICAN COLLEGE of CARDIOLOGY

Objective: To evaluate dapagliflozin (a sodium-glucose cotransporter 2 [SGLT2] inhibitor) compared with placebo among patients with heart failure and a reduced ejection fraction (HFrEF).

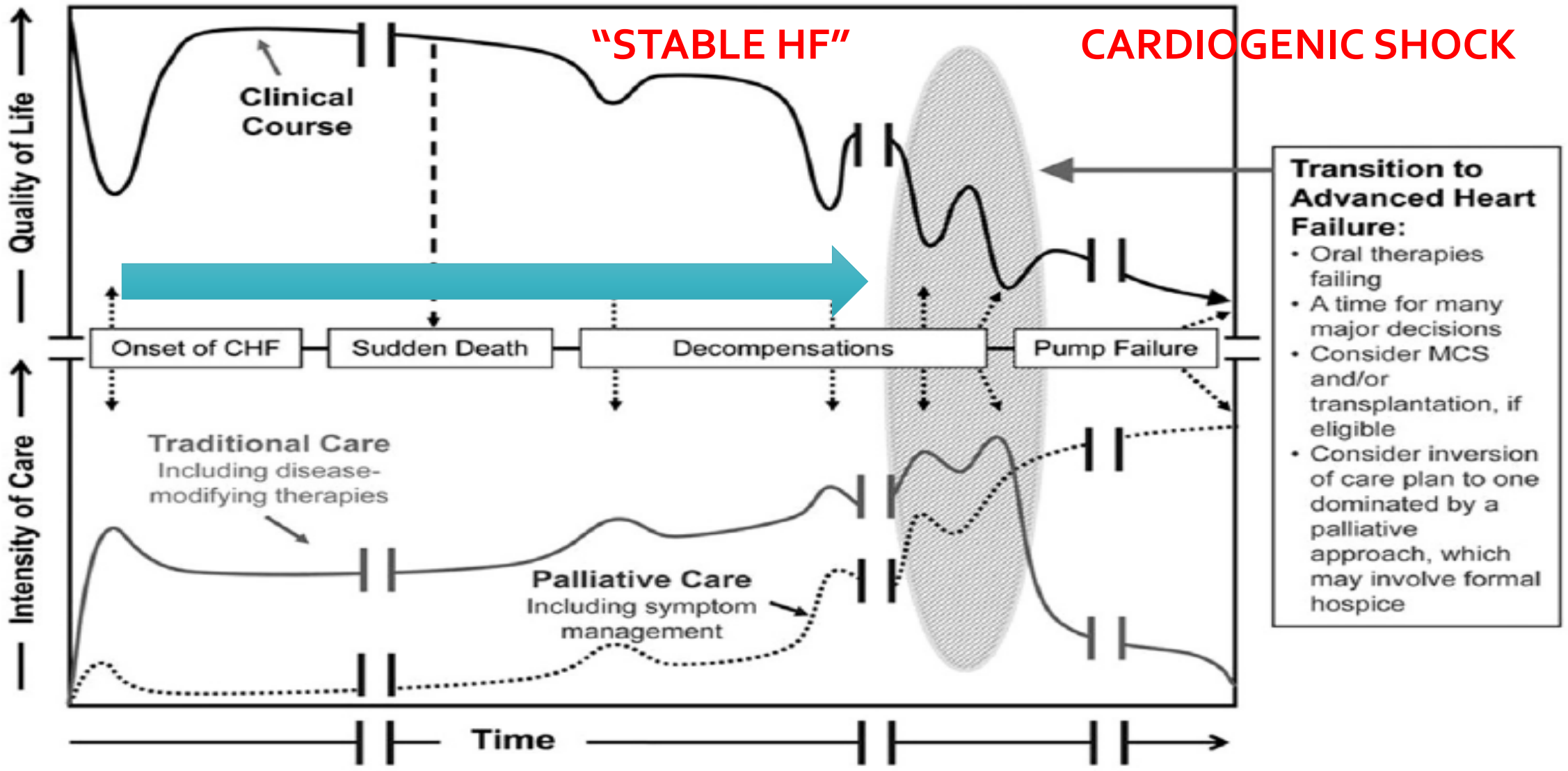
Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies on All Cause Mortality

	Relative Risk	2 Year Mortality
None	- -	35.0%
ARNI (vs imputed placebo)	↓ 28%	25.2%
Beta Blocker	↓ 35%	16.4%
Aldosterone Ant	↓ 30%	11.5%
SGLT2 inhibitor	↓ 17%	9.5%

Cumulative risk reduction in mortality if all evidence-based medical therapies are used:
Relative risk reduction 72.9%, Absolute risk reduction: 25.5%, NNT = 3.9

Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196.

PROGRESSION OF HEART FAILURE



Circulation 2012;125(5):1930.

Advanced Heart Failure/Cardiogenic Shock

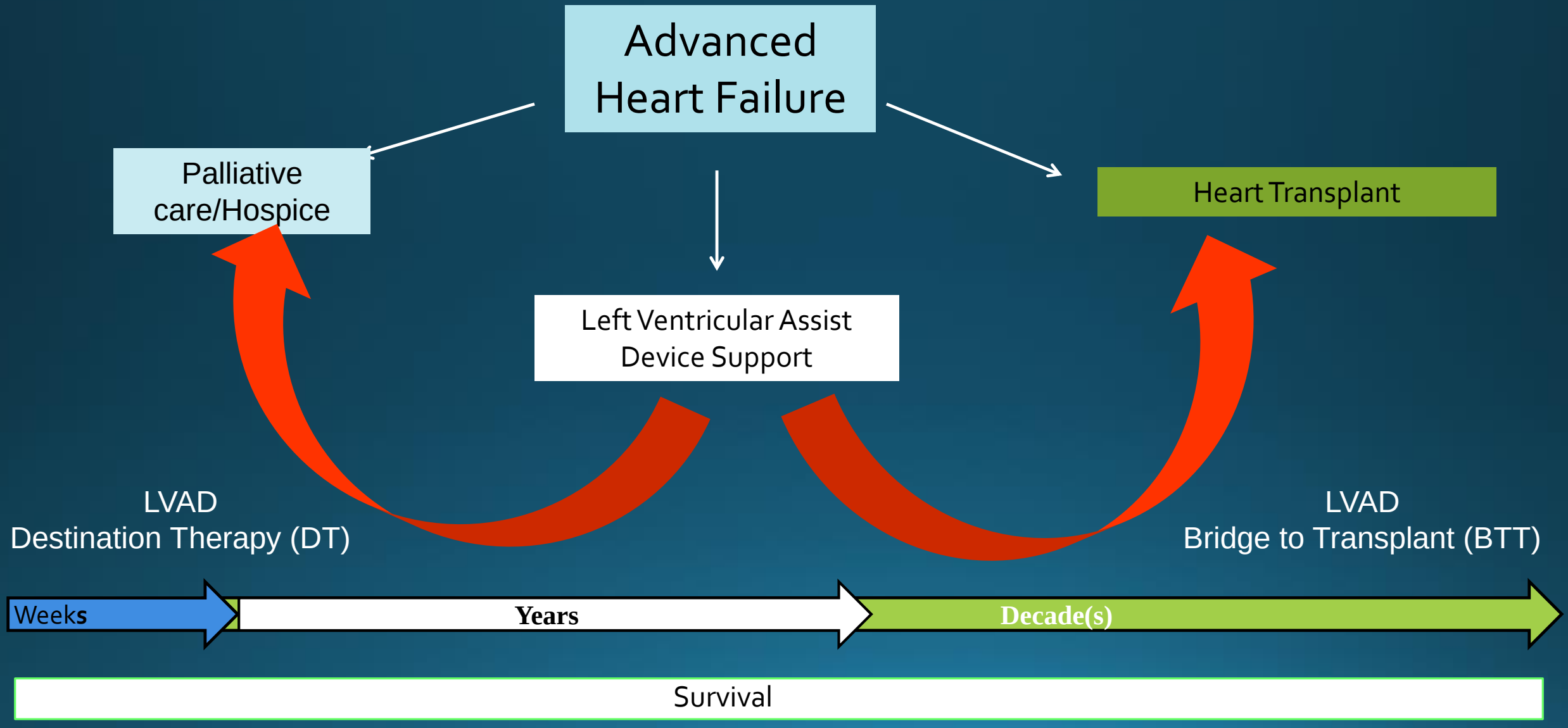
Clinical criteria

- Hypotension:
  - Systolic blood pressure (SBP) less than 90 mm Hg for at least 30 minutes or Need for supportive measures to maintain an SBP greater than or equal to 90 mm Hg
- End-organ hypo perfusion:
  - Cool extremities or
  - Urine output less than 30 mL/h and
  - Heart rate greater than 60 beats/min

Hemodynamic criteria

- Cardiac index less than or equal to 2.2 L/min/m2 and
- Pulmonary capillary wedge pressure greater than or equal to 15 mm Hg

Management Pathways



HEART TRANSPLANTATION

ELSEVIER

50 YEAR ANNIVERSARY

DEC 2017

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

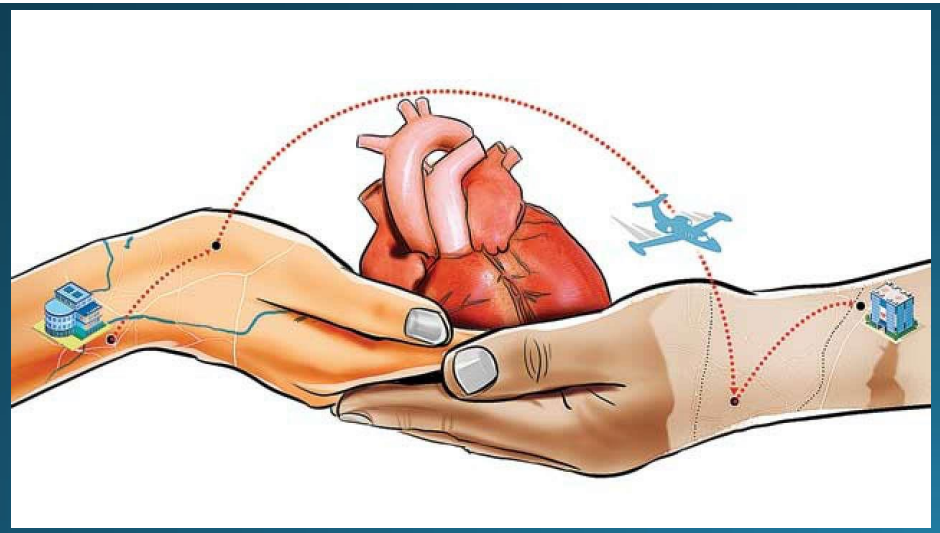
PIONEERING PERSPECTIVES

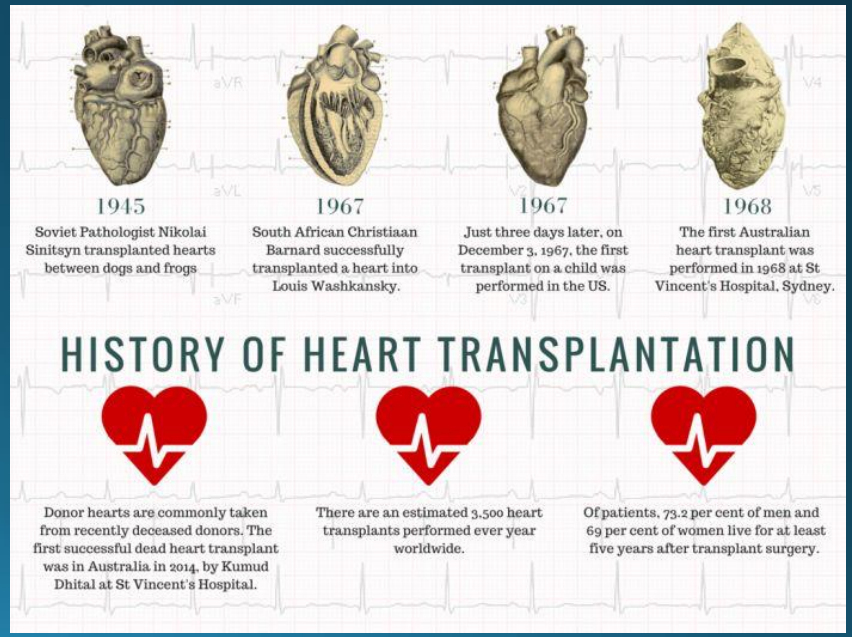
Life's defining moment: Christiaan Barnard and the first human heart transplant

CrossMark

David K.C. Cooper, MD, PhD

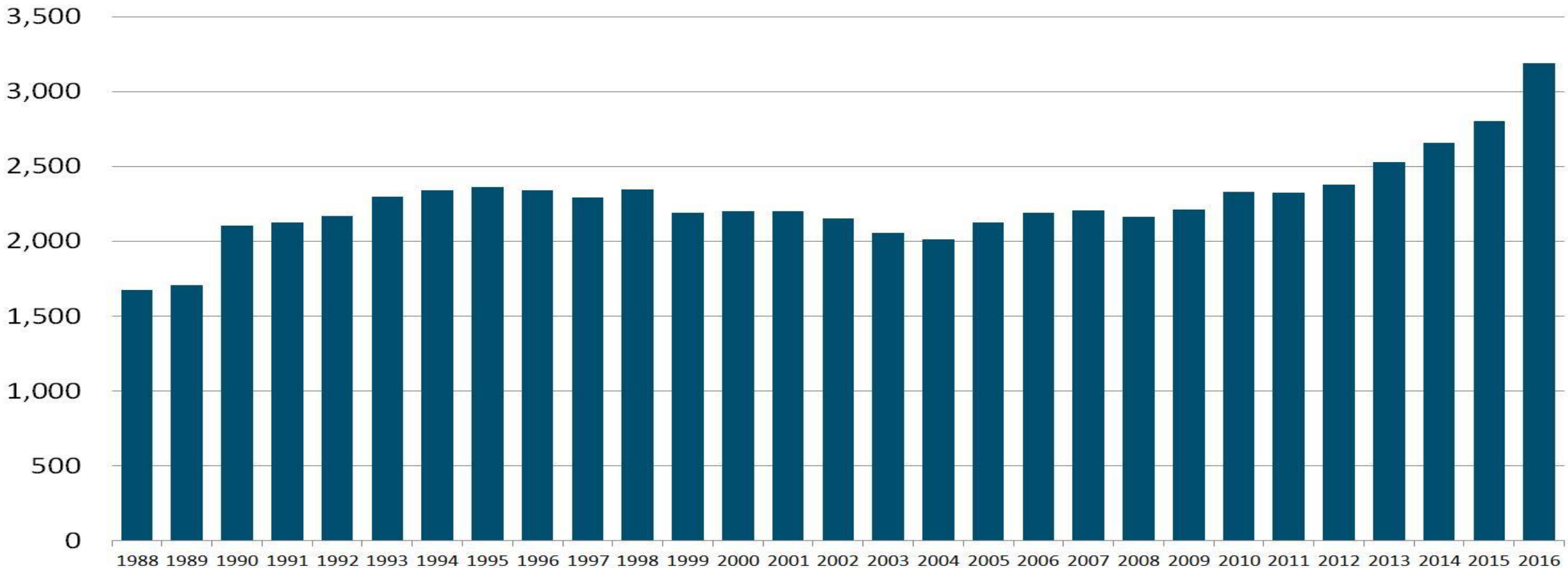
From the Xenotransplantation Program, Department of Surgery, University of Alabama at Birmingham, Birmingham, Alabama, USA.





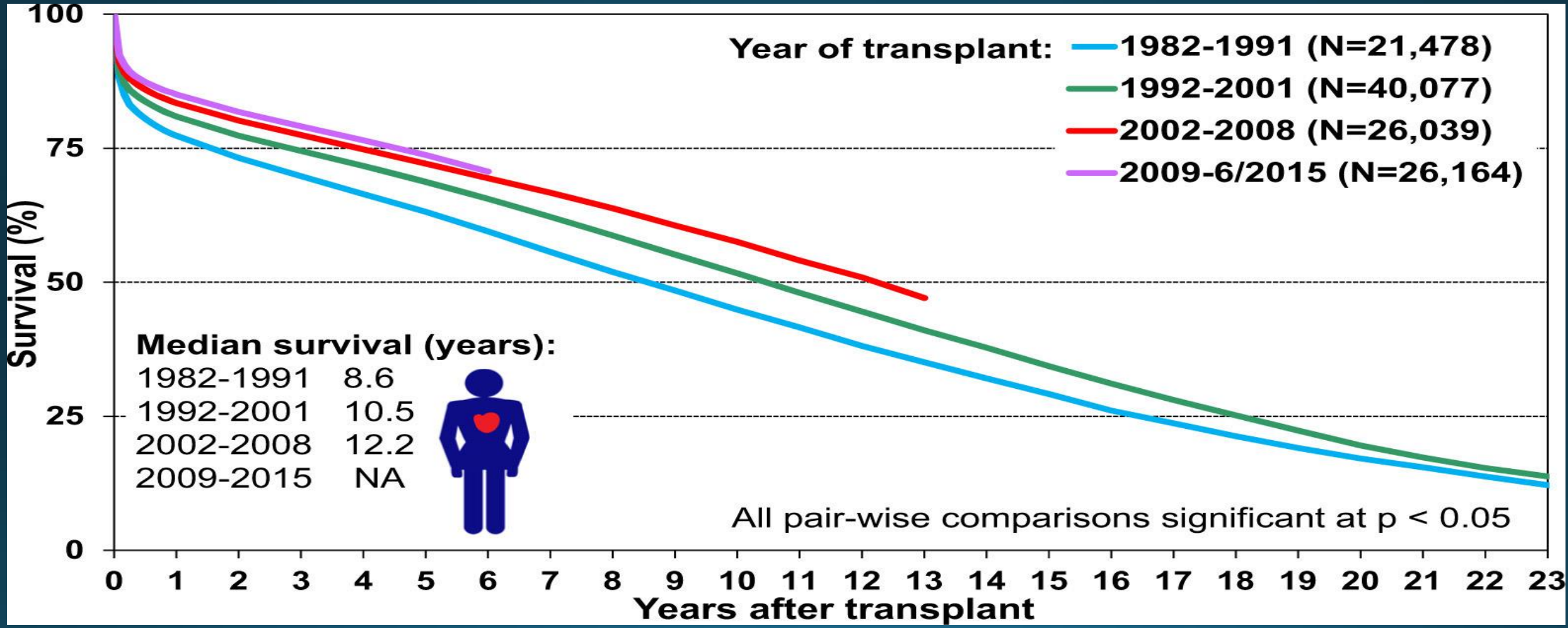
The prevalence of heart failure continues to grow, but the number of transplants has remained limited[1,2]

NUMBER OF HEART TRANSPLANTS REPORTED PER YEAR[1]



References: 1. UNOS (United Network for Organ Sharing). Heart Transplants, 1988-2016. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/# (Accessed Aug. 8, 2017). **2.** Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. *Nat Rev Cardiol.* 2011;8(1):30-41.

SURVIVAL WITH HEART TRANSPLANT



The Journal of Heart and Lung Transplantation 2017 36, 1037 1046DOI: (10.1016/j.healun.2017.07.019)

Transplant Listing Candidacy

CONSIDERATIONS:

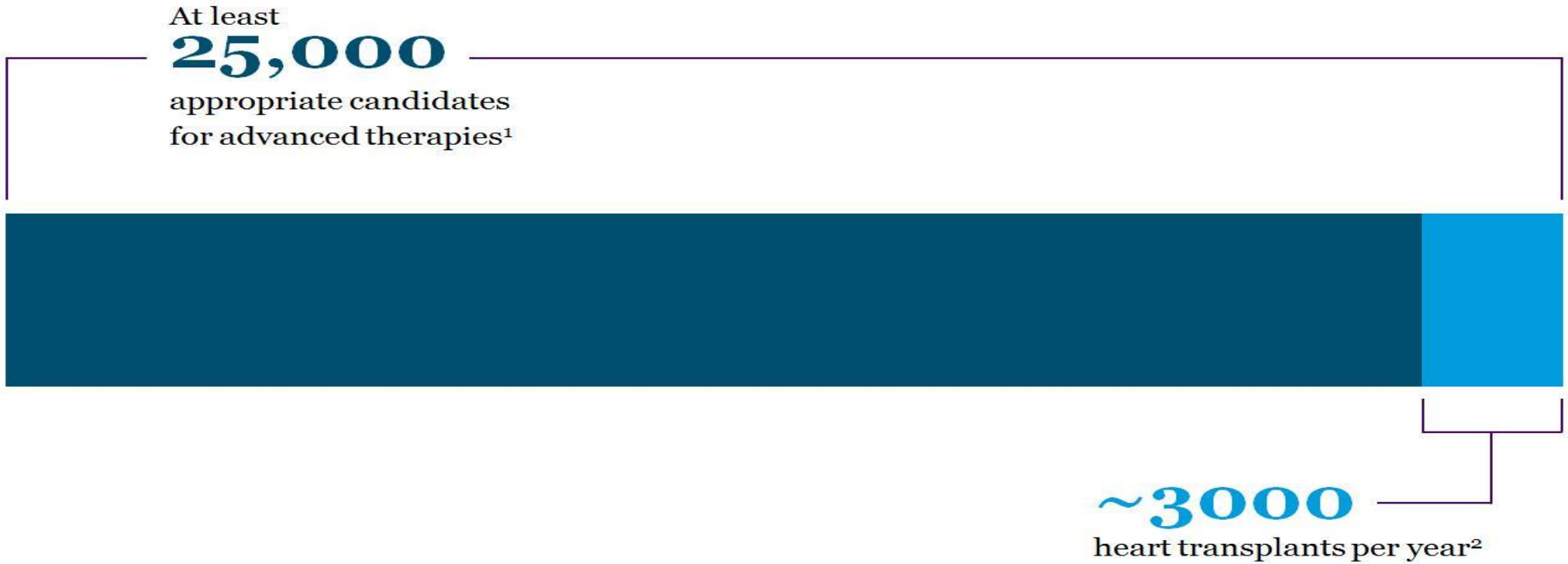
- Age: <70 years; not absolute
- Cancer free >5 years
- Obesity: BMI ≤35 kg/m^2
- Severity of other medical comorbidities
  - Renal Function (Cr <1.8 mg/dL) or dual organ transplant….
  - Cirrhosis (cardiac or otherwise)
  - Functional status
  - Nutritional status
  - Diabetes control (HgA1C <7.5)
  - COPD

Transplant Listing Candidacy

- Social:
  - No substance abuse: includes THC and ETOH (6 months tox free)
  - No tobacco abuse: 6 months free
  - Good family support system
- $$: can they afford meds???
- Adherence to medical follow-up

HIGHLY Selected Patients

Transplantation is considered the gold standard, but the supply of donor hearts is limited[1,2]



References: **1.** Dunlay SM, Roger VL. Understanding the epidemic of heart failure: past, present, and future. *Curr Heart Fail Rep*. 2014;11(4):404-415. **2.** UNOS (United Network for Organ Sharing). Heart Transplants, 1988-2016. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/# (Accessed Aug. 8, 2017).

FINAL NEW YORK STOCKS
(See Financial Pages)

The Times

SAN MATEO TIMES AND DAILY NEWS LEADER

WEATHER
Fair tonight and Friday. Low temperature tonight, 42 degrees; high Friday, 68. West to northwesterly winds, 10 to 20 miles per hour in the afternoon.

Vol. 66 — No. 95 ★ ★ ★—C 4 Sections 48 PAGES

10c PER COPY — $2.00 PER MONTH

APRIL 21, 1966

Artificial Heart Keeping Man Alive

OVER PENINSULA

Strange Light Was Caused By a Rocket

Human Bone Intensifies Clue Search

Pacifist Group Is Defiant

By AP and UPI

MECHANICAL HEART INSTALLED — Dr. Michael Debakey, noted heart surgeon, gets ready to connect the mechanical heart to his patient, Marcel L. DeRudder, at Methodist Hospital in Houston today. Assisting surgeon at left not identified. (See AP Wire Story) (AP Wirephoto)

Doctors Say Patient, 65, 'Looks Good'

HOUSTON (UPI)—Famed surgeon Dr. Michael DeBakey today attached an artificial heart to a 65-year-old patient in a medical breakthrough and used the machine plus emergency massage in a successful life-or-death operation.

Approximately three hours after the surgery began, Marcel L. De Rudder, a coal miner from Westville, Ill., was "looking good" on the operating table and the artificial heart was pumping 86 times a minute with a steady "thump" not unlike that of the human heart.

Surgery lasted more than five hours. It began at 7:30 a.m. CST and the chest was closed shortly after 1:30 p.m. CST.

Attendants prepared to wheel De Rudder from the turquoise-tinted operating room to the intensive care unit.

Ventricular Assist Device (VAD)

A mechanical circulatory device used to partially or completely replace the function of either the left ventricle (LVAD); the right ventricle (RVAD); or both ventricles (BiVAD)

Long-Term VAD

DURABLE

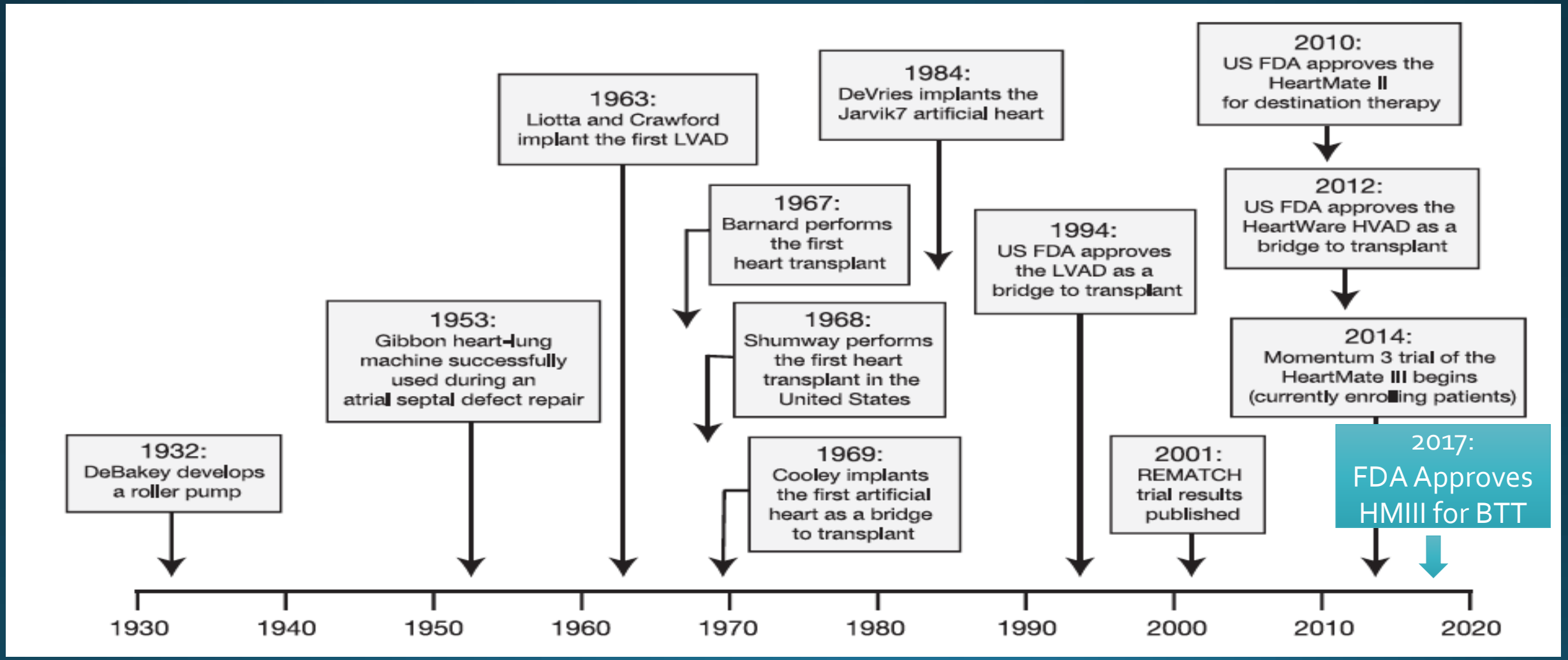
Implanted surgically with the intention of support for months to years

Short-Term VAD

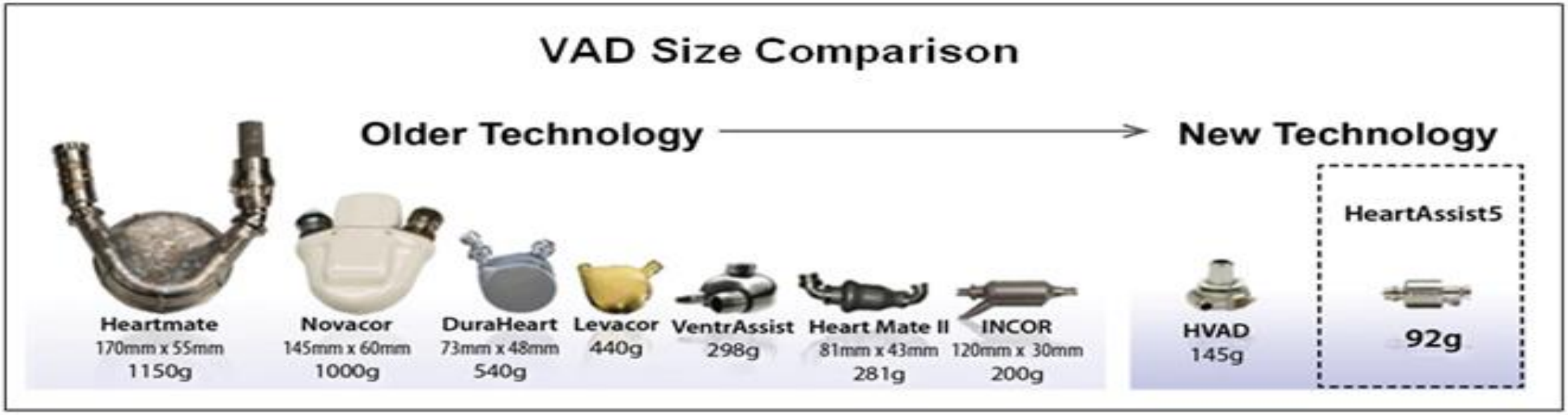
Temporary

Utilized for urgent/ emergent support over the course of days to weeks

Landmark events in the development of left ventricular assist devices

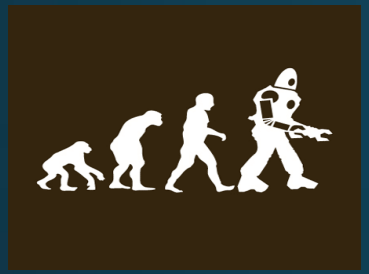


VAD Size Comparison



Getting bigger by getting smaller

Procedure	Surgical	Minimally Invasive	Catheter Delivery System
Flow	10 L/min	7 L/min	3 L/min
Patient Class	Late Class IV	Class III & IV	Class III
Treatable Pop.	100,000	350,000	1,000,000
Current status:	IDE	Preclinical studies	Prototype and exploratory



LVAD Evolution

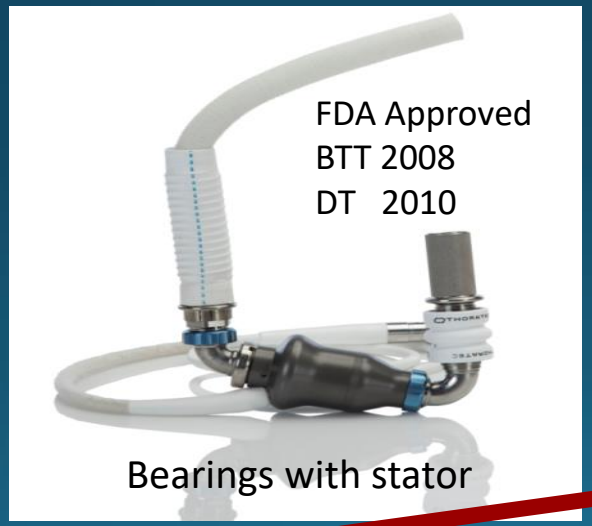
- Miniaturization
- Durability

Pulsatile Technology

1st Generation

Continuous Flow Technology
Axial Design

2nd Generation



Continuous Flow Technology
Centrifugal Design

3rd Generation

Bearingless with magnetic levitation

Durable MCS

Bridge to Transplantation (BTT)

- Patient is approved and currently listed for transplant
- NYHA IV
- Failed maximized medical therapy

Destination Therapy (DT)

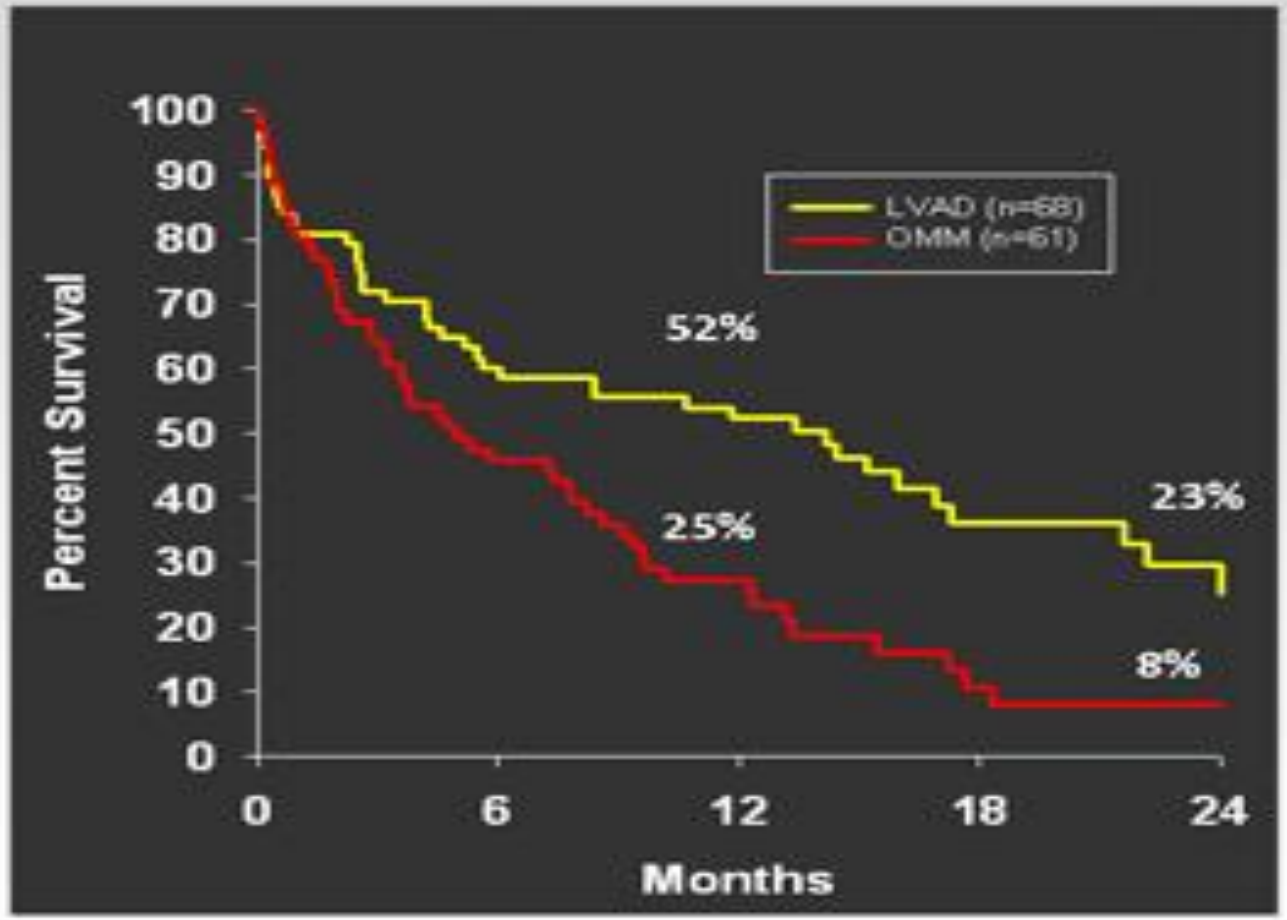
- Not a heart transplant candidate
- NYHA IV
- LVEF <25%
- Maximized medical therapy >45 of 60 days; IABP for 7 days; OR inotropic support for 14 days
- Functional limitation with a peak oxygen consumption of less than or equal to 14 ml/kg/min

http://www.cms.gov/medicare-coverage-database

REMATCH

Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure

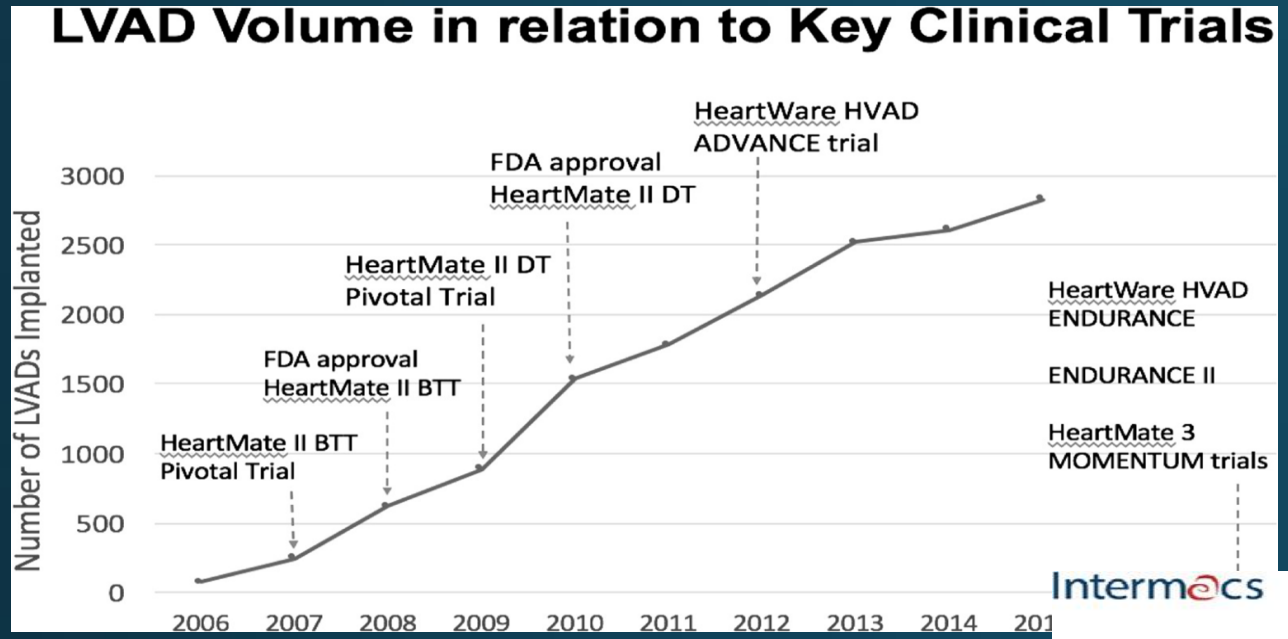
- Randomized clinical trial
  - Optimal medical therapy vs pulsatile flow LVAD
- Nontransplant candidates (n = 129)
  - EF ≤ 25%
  - Peak VO2 < 12 mL/kg/min
  - Or continuous infusion inotropes
- FDA approval for XVE as destination therapy

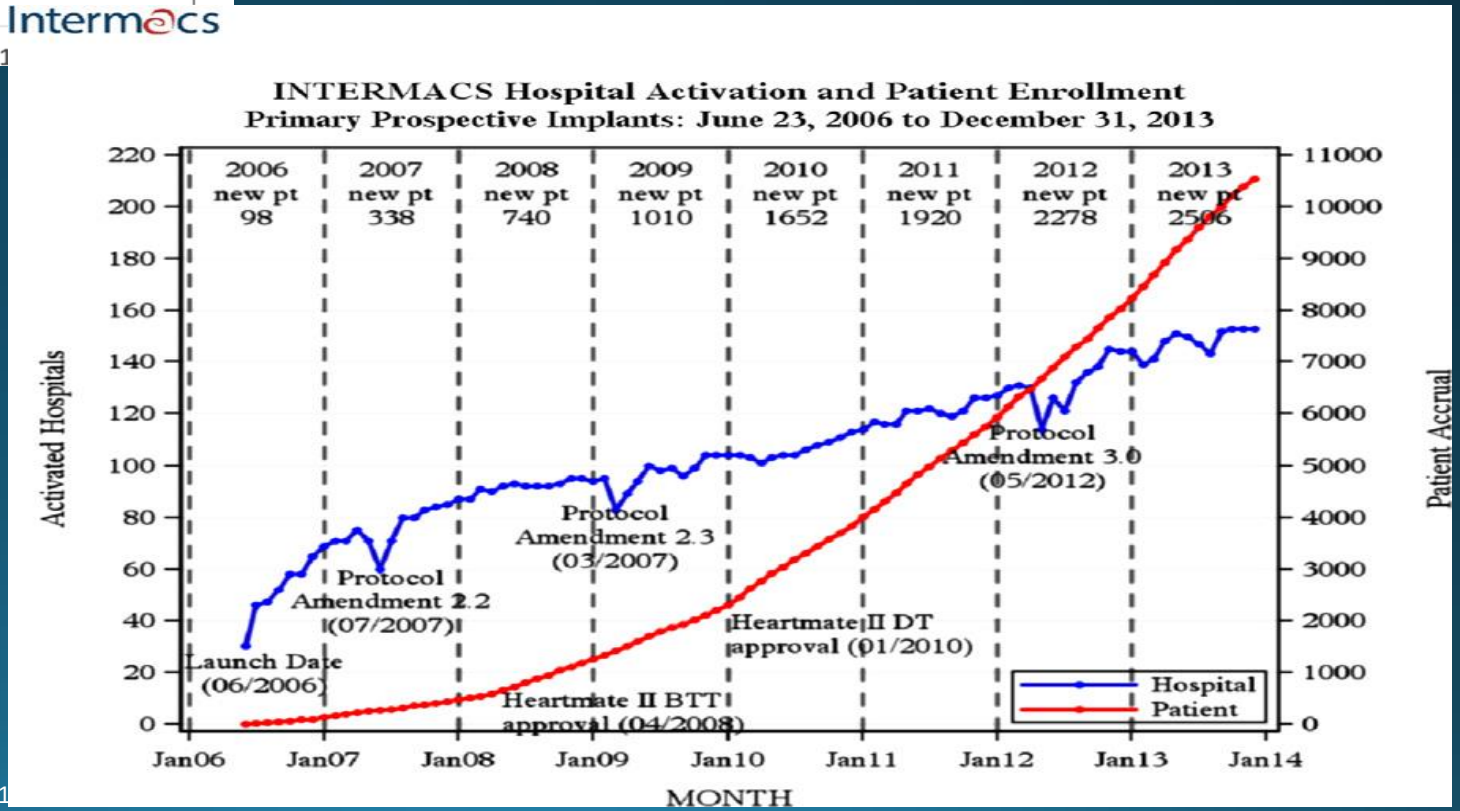


Heart failure

Rose EA, et al. *N Engl J Med*. 2001;345:1435-1443.

theheart.org MedscapeCME

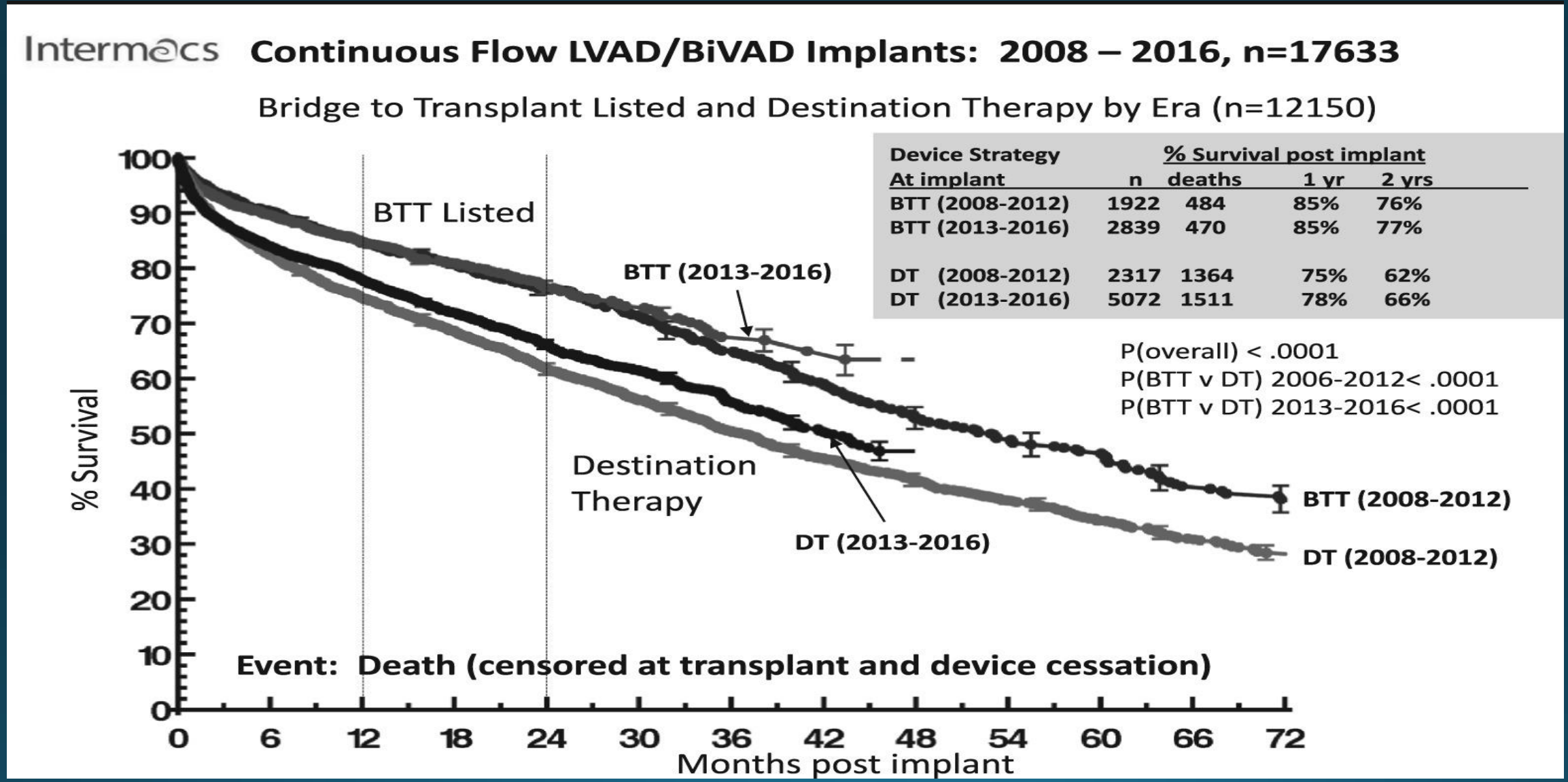




The Journal of Heart and Lung Transplantation DOI: (10.1016/j.healun.201

Why LVAD use has increased?

- Organ donor shortage with rising HF prevalence
- Improved survival on the transplant waiting list
- In selected patients (elderly, high risk transplants), LVAD is preferable to transplant to better utilize "limited resource" of donor organs
- Destination Therapy



The Journal of Heart and Lung Transplantation 2017 36, 1080 1086DOI: (10.1016/j.healun.2017.07.005)

Home Inotropic support

- Palliative Care- comfort
- Bridge to decision/Therapy (MCS, Transplant)

When to Refer

Outpatients:

- ≥2 admissions for CHF in a year and LVEF <25%
- Abnormal labs: ↑Cr ↓NA
- Inability to titrate CHF Meds due to hypotension
- Escalating diuretic needs (>80 mg lasix QD) or need for primer
- >1 ICD discharge for VT in a year

When to Refer

Inpatients:

- End organ dysfunction:
- ↑ALT, ↑ Bili, ↑Cr, ↑INR off warfarin
- Need for ventilator or balloon pump support
- Need for:
  - ≥ inotropes
  - Vasopressor
- Low EF and poor surgical candidate: LVEF ≤25% with CAD, dilated LV (LViDd >65 mm), RV dysfunction, or pulmonary HTN

I NEED HELP

- **I** – Inotropes
- **N** – NYHA IIIB/IV or Persistently elevated natriuretic peptide
- **E** – End Organ Dysfunction
- **E** – EF < 35%
- **D** – Defibrillator shocks
- **H** – Hospitalization > 1
- **E** – Edema despite escalating diuretics
- **L** – Low BP, High HR
- **P** – Prognostic medication, progressive intolerance or down-titration of GDMT

TRIGGERS FOR HF PATIENT REFERRAL TO HF PROGRAM (OR SPECIALIST)

- New onset HF
- Chronic HF with high risk features
- To assist with managing guideline directed medical therapy (GDMT)
- Persistently reduced LVEF (< 35%) despite GDMT for > 3 months
- Need 2nd opinion
- Annual review for established HF patients with advanced disease
- Participation in a clinical trial

Yancy CW, Januzzi JL Jr, Allen LA, Butler J, Davis LL, & et al 2017 ACC expert consensus decision pathway for optimization of HF treatment: answers to 10 pivotal issues about HF with reduced EF: a report of the ACC Task Force on Clinical Expert Consensus Decision Pathways. J Am Coll Cardiol 2017;71

10 Principles for Successful Treatment of Heart Failure

2017 ACCF/AHA Heart Failure Guidelines

How to implement GDMT...

I. Initiate & Switch

Treatment algorithm for guideline-directed medical therapy including novel therapies (*Figure 2* and *3*)

II. Titration

Target doses of select guideline-directed heart failure therapy (*Tables 1, 2, 3, 4, 5*)

Considerations for monitoring

How to address challenges with...

III. Referral

Triggers for referral to HF specialist (*Table 6*)

IV. Care Coordination

Essential skills for a HF team (*Table 7*)

Infrastructure for team-based HF care (*Table 8*)

V. Adherence

Causes of non-adherence *(Table 9)*

Interventions for adherence *(Table 10, 11)*

VI. Specific Patient Cohorts

Evidence based recommendations and assessment of risk for special cohorts: African Americans; older adults; frail (*Table 12*)

VII. Cost of Care

Strategies to reduce cost (*Table 13*)

Helpful information for completion of prior authorization forms (*Table 14*)

How to manage...

VIII. Increasing Complexity

Ten pathophysiologic targets in HFrEF and treatments (*Table 15*)

Ten principles and actions to guide optimal therapy

IX. Comorbidities

Common cardiac and non-cardiac comorbidities with suggested actions (*Table 16*)

X. Palliative/Hospice Care

Seven principles and actions to consider regarding palliative care

Summary

- The management of heart failure is a dynamic process that requires frequent re-evaluation
- MCS and Transplant have shown to improve mortality rates AND quality of life
- EARLY Referral is the key!