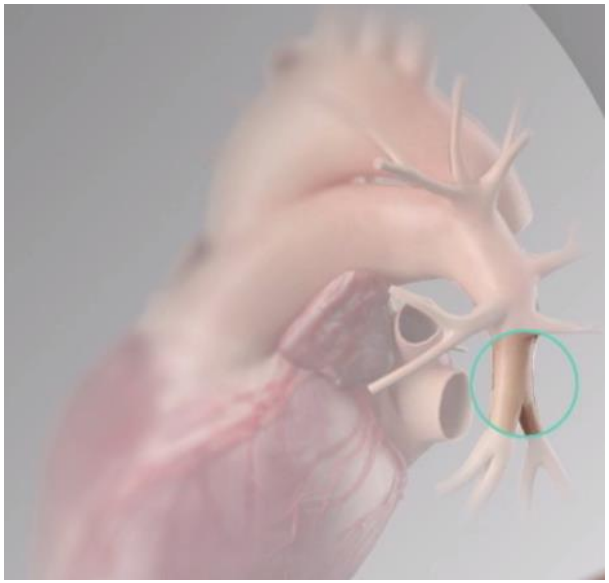
Home monitors for PA pressure in HF patients



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Heart Failure – A Growing Global Concern

Prevalence and Incidence

- Overall 2.1% prevalence: over 23 million worldwide
- > 650,000 people newly diagnosed each year with HF

Mortality

– For AHA/ACC stage C/D patients diagnosed with HF:

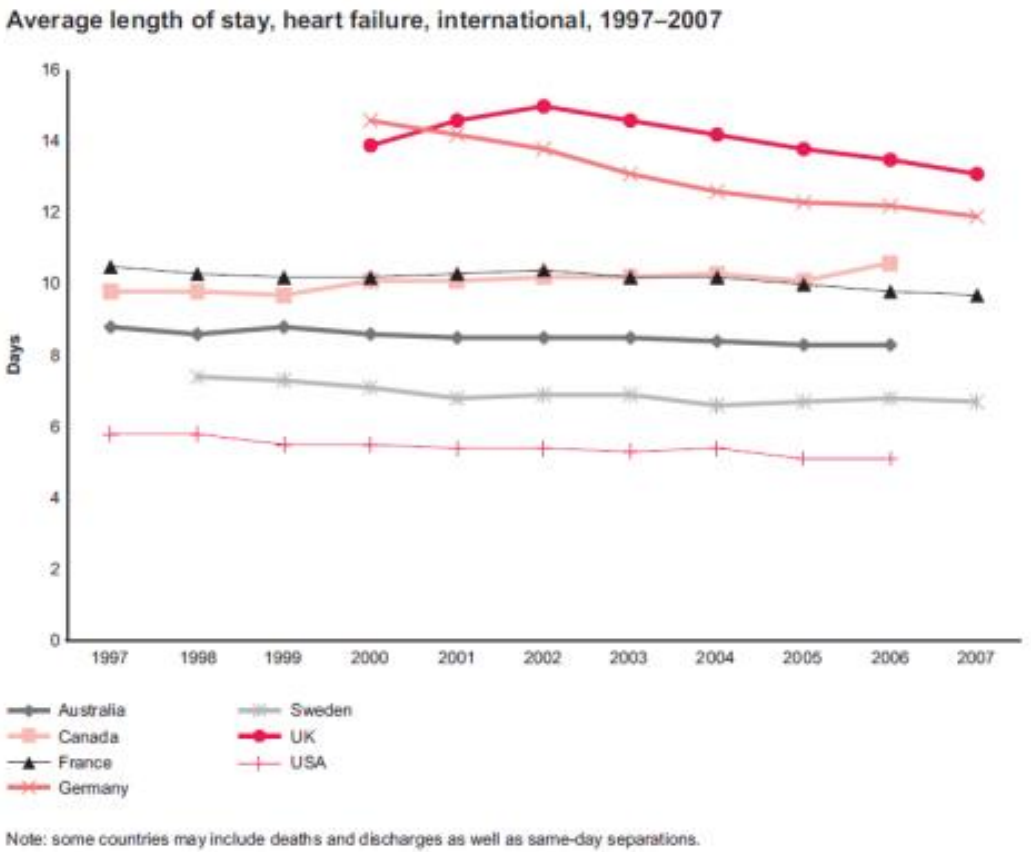
- 30% will die in the first year
- 60% will die within 5 years

HF prevalence in the US is projected to increase 46% from 2012 to 2030, resulting in > 8M people ≥ 18 years of age with HF.[6]

Circ Res. 2013;113:646–659.

Heart Failure Is Associated with High Hospitalization and Readmission Rates

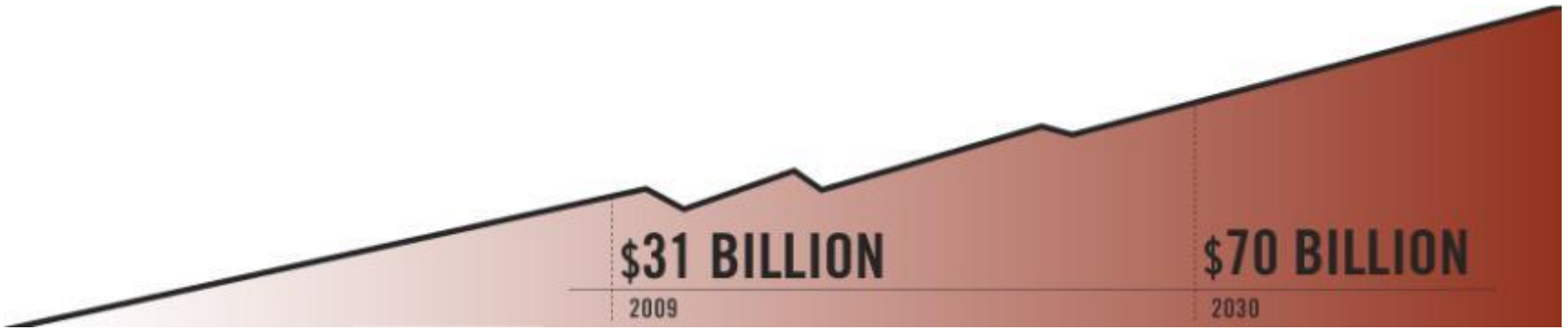
- Average length of hospital stay
  - Approximately 5 days (US)
  - 11 days (Europe)
- HF is also associated with high readmission rates:
  - ~25% all-cause readmission within 30 days
    and ~50% within 6 months



Yancy et al. JACC, 2006.

Economic Burden of HF Will Continue to Rise Through 2030

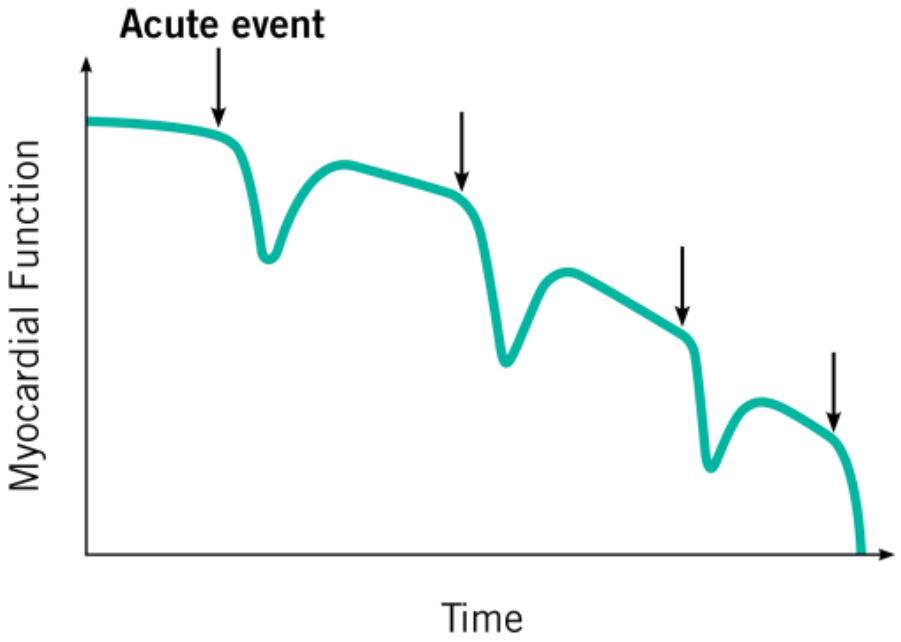
- The AHA estimates that the total medical costs for HF are projected to increase to $70B by 2030 → a 2-fold increase from 2013.
- 50% of the costs are attributed to hospitalization.



Graph: Heidenreich PA, et al. Circulation Heart Failure 2013.

Worsening Heart Failure Leading to HF Hospitalizations Contributes to Disease Progression

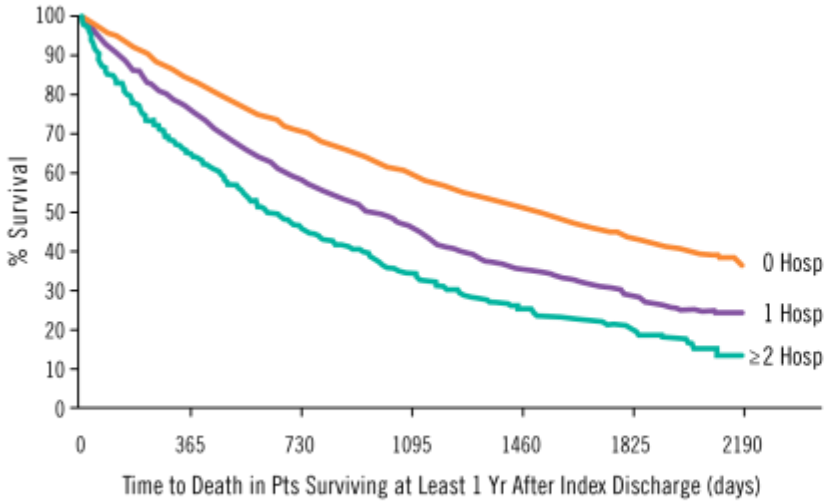
With each subsequent HF-related admission, the patient leaves the hospital with a further decrease in cardiac function.



Graph adapted from: Gheorghiade MD, et al. Am J. Cardiol. 2005

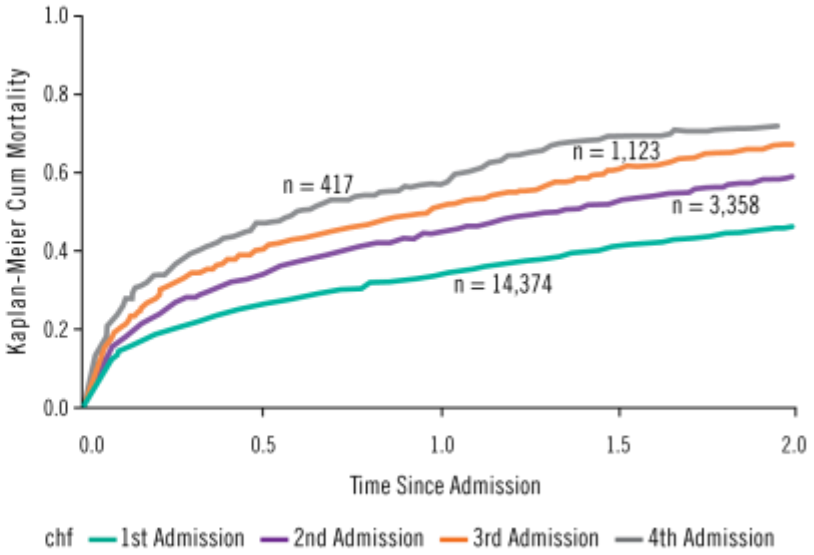
HF Hospitalizations are a Strong Predictor of Mortality

Data from the EFFECT study, n = 9138 patients



Among 1 year survivors after index EFFECT-HF discharge, the number of heart failure hospitalizations in the preceding year stratified the risk of death in crude analysis.[1]

Data from Setoguchi et al., n = 14,374 patients[2]



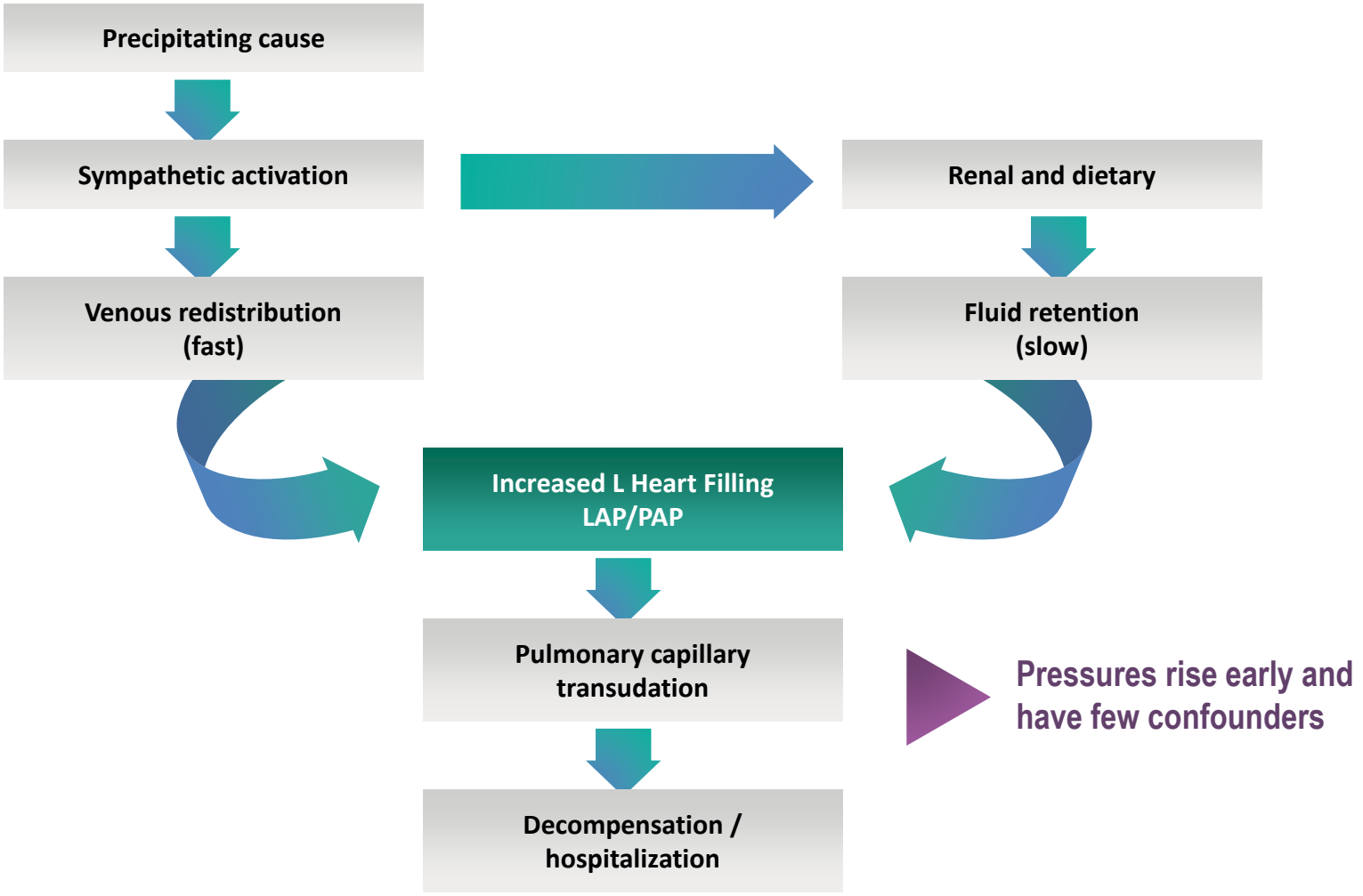
KP cumulative mortality curve for all-cause mortality after each subsequent hospitalization for HF.[2]

Studies show each admission decreases a patient's chance of survival.

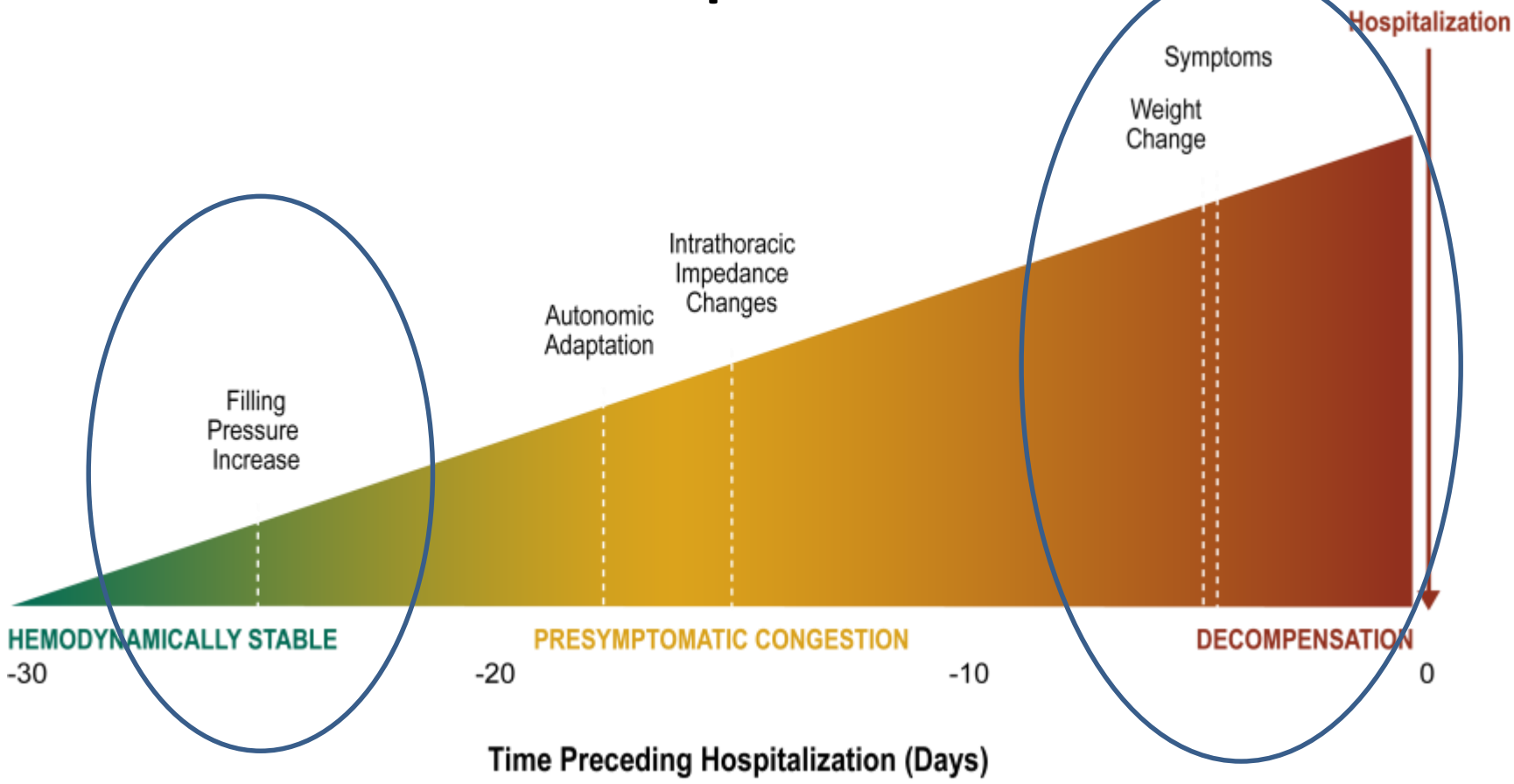
Lee DS, et al. Am J of Med, 2009.
Setoguchi S, et al. Am Heart J, 2007.

Mechanisms of Worsening Heart Failure

Increased pressure is the proximate cause of congestion



Physiologic Markers of Acute Decompensation



Graph adapted from Adamson PB, et al. Curr Heart Fail Reports, 2009.

Clinical Examination has Limited Reliability in Assessing Filling Pressures

Data from clinical evaluations has poor sensitivity and predictive value in determining hemodynamic profile

Capomolla, 2005. N = 366

Variable	Estimate of	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
JVP	RAP	48	78	60	69
Edema		10	94	55	60
Pulse Press	Cardiac Index	27	69	52	44
S3	PCWP	36	81	69	54
Dyspnea		50	73	67	57
Rales		13	90	60	48

Table adapted from Capomolla S, et al. Eur J Heart Failure, 2005.

TIM-HF Trial: Telemonitoring of Weight and Blood Pressure Do Not Reduce Readmission or Mortality

- Randomized study of 710 patients
- Primary Endpoint: Total Mortality
- Control Group: Standard-of-care (no telemonitoring)
- Treatment Group: Telemonitoring of weight and BP information
- **Results: No difference in all-cause death or HF hospitalizations**

End Point	Telemonitoring n = 354 (%)	Usual care n = 356 (%)	HR (95% CI)	p
All-cause mortality	15.3	15.4	0.97 (0.67-1.41)	0.87
Cardiovascular-related mortality	11.3	12.9	0.86 (0.56-1.31)	0.49
All-cause readmission	54.2	50.3	1.12 (0.91-1.37)	0.29

Koehler F et al, Circulation 2011

Cardiac implanted electronic devices for heart failure monitoring

Electrophysiological Sensors

- Most commonly pacemaker and defibrillator.
- They have the capability of sensing certain atrial and ventricular arrhythmias.
- Heart rate variability

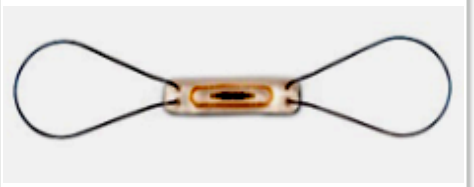
  -standard deviation of 5-minute median atrial-atrial intervals (SDAAM) or consecutive ventricular (N-N) intervals (SDANN) over a 24-hour period.
- Detect HRV as early as three weeks before hospitalization

Hemodynamic Monitoring Sensors

- Chronicle (right ventricular pressure)
- ePOD (estimated pulmonary artery diastolic pressure)
- Heart PAD (left atrial pressure)
- CardioMEMS™ (pulmonary artery pressure)

CardioMEMS™ HF System

Pulmonary Artery Pressure Sensor

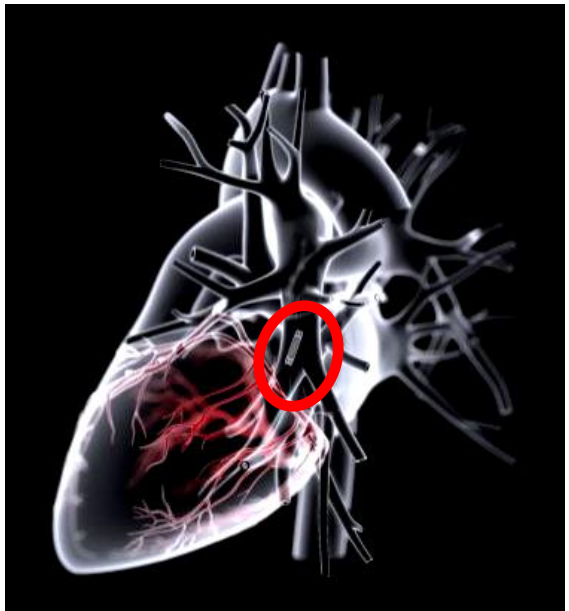


Patient Electronics System

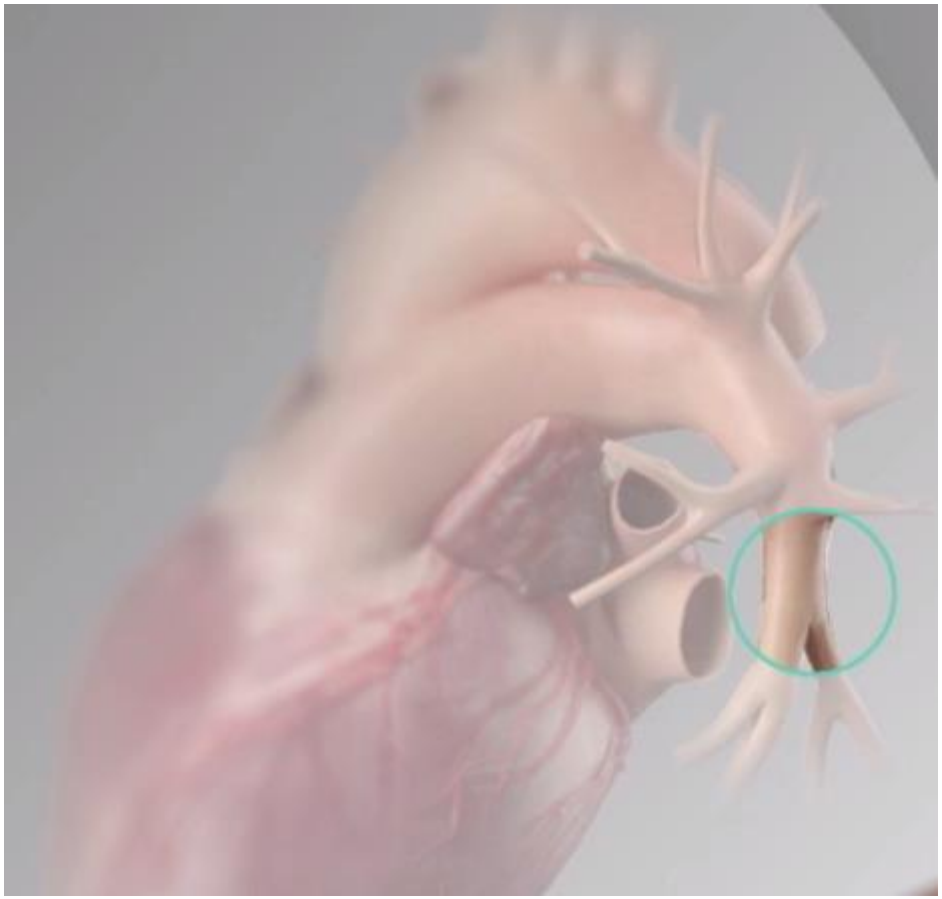
CardioMEMS™ HF System Website

CardioMEMS™ HF System

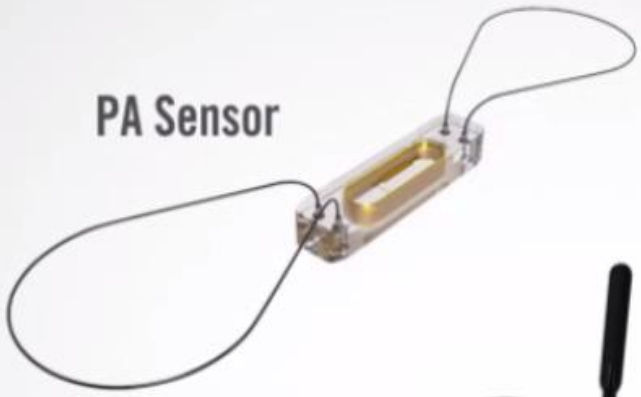
- CardioMEMS™ is a wireless device that monitors PAP.
- PAP measured by CardioMEMS™ device correlates with PAP measured by Swan-Ganz and echocardiography



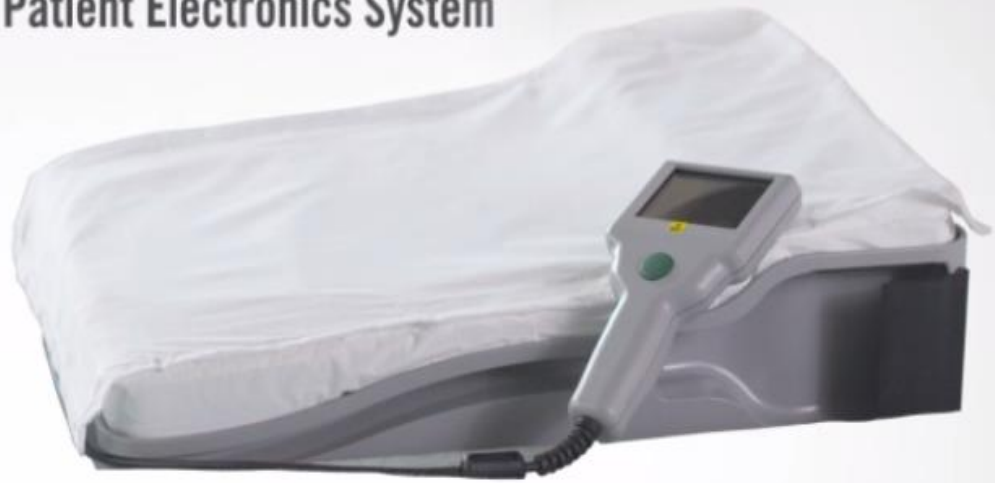
- It is implanted in the distal pulmonary artery via an RHC.

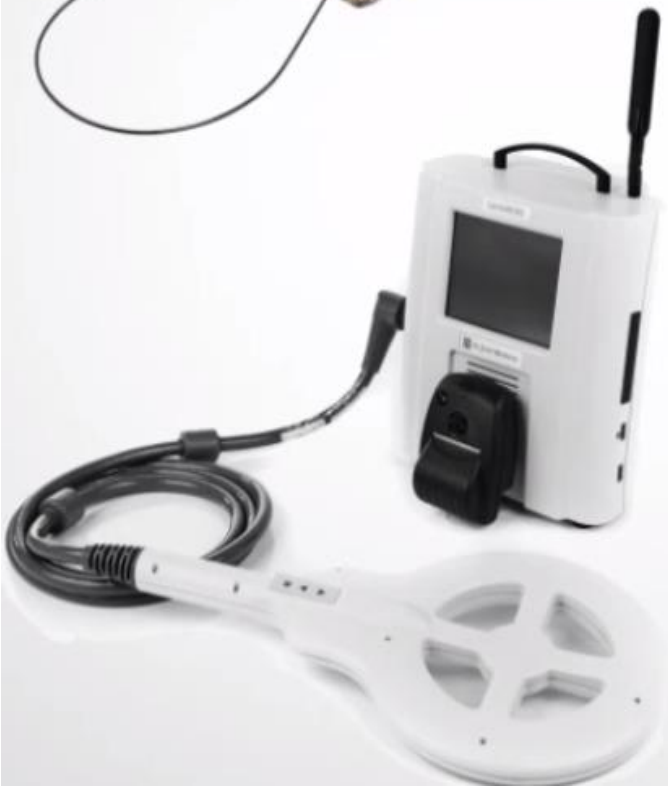


PA Sensor



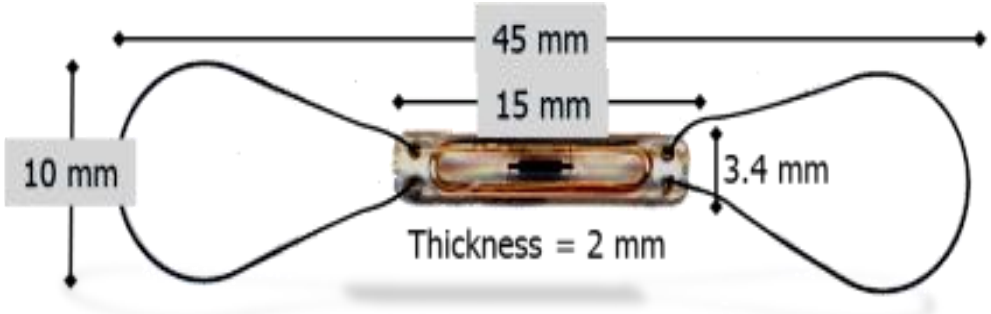
Patient Electronics System

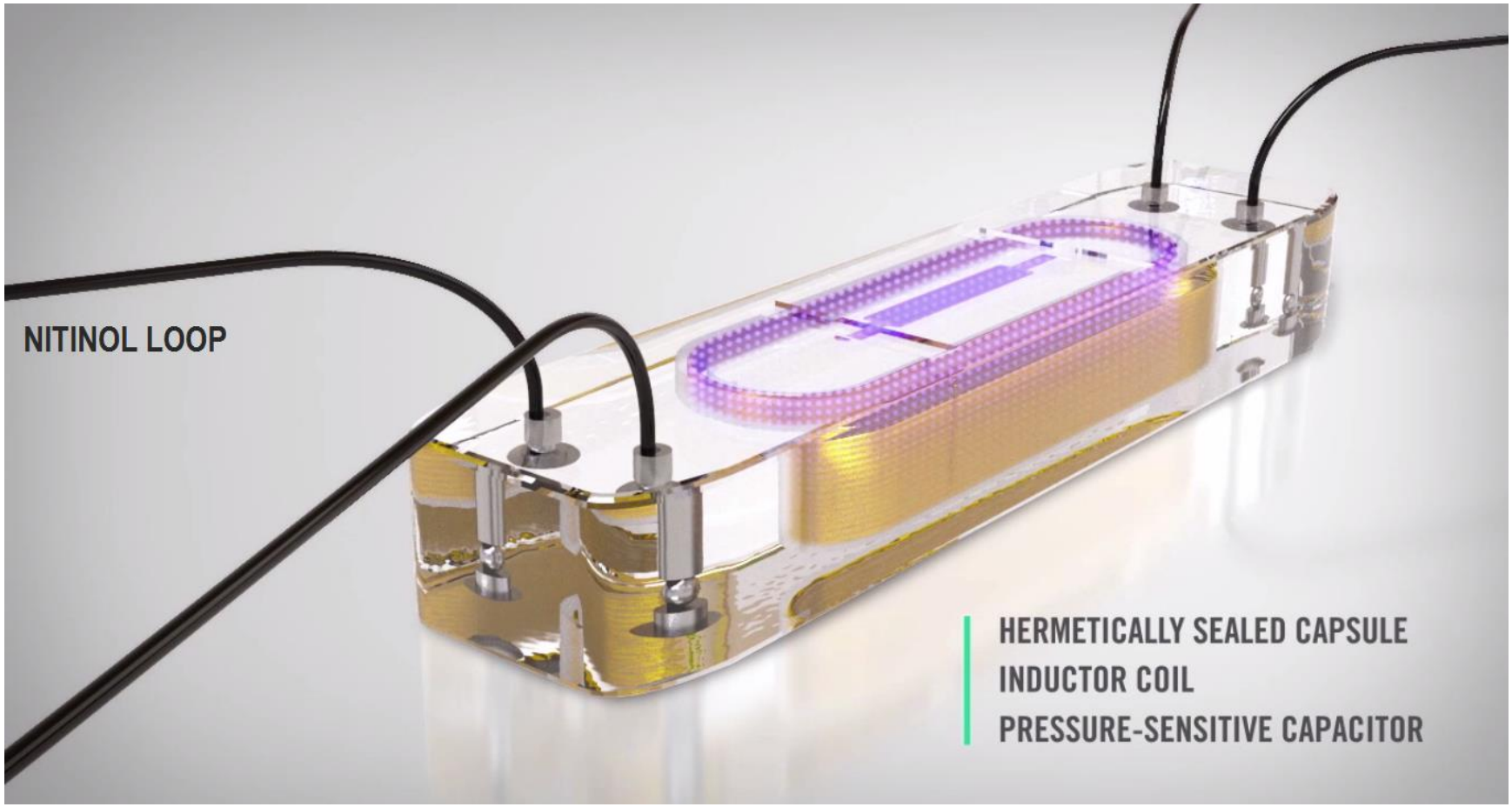


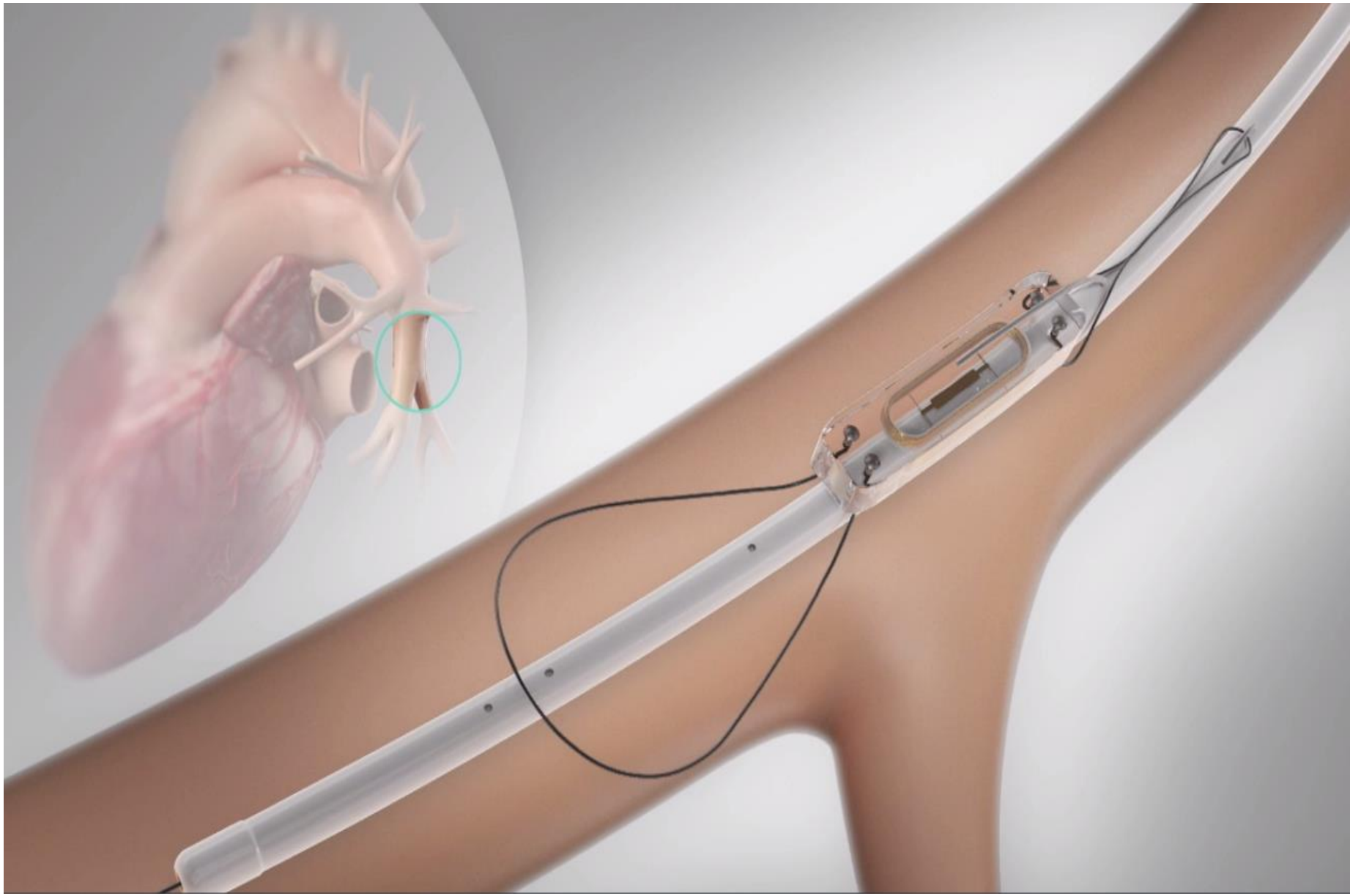


Hospital
Electronics
System

Delivery Catheter


45 mm
15 mm
10 mm
3.4 mm
Thickness = 2 mm


NITINOL LOOP
HERMETICALLY SEALED CAPSULE
INDUCTOR COIL
PRESSURE-SENSITIVE CAPACITOR



In 2014 the FDA approved the use of CardioMEMS™ sensor implant in patients with HFpEF and HFrEF with NYHA class III on optimal medical therapy and a history of HFH within the last year

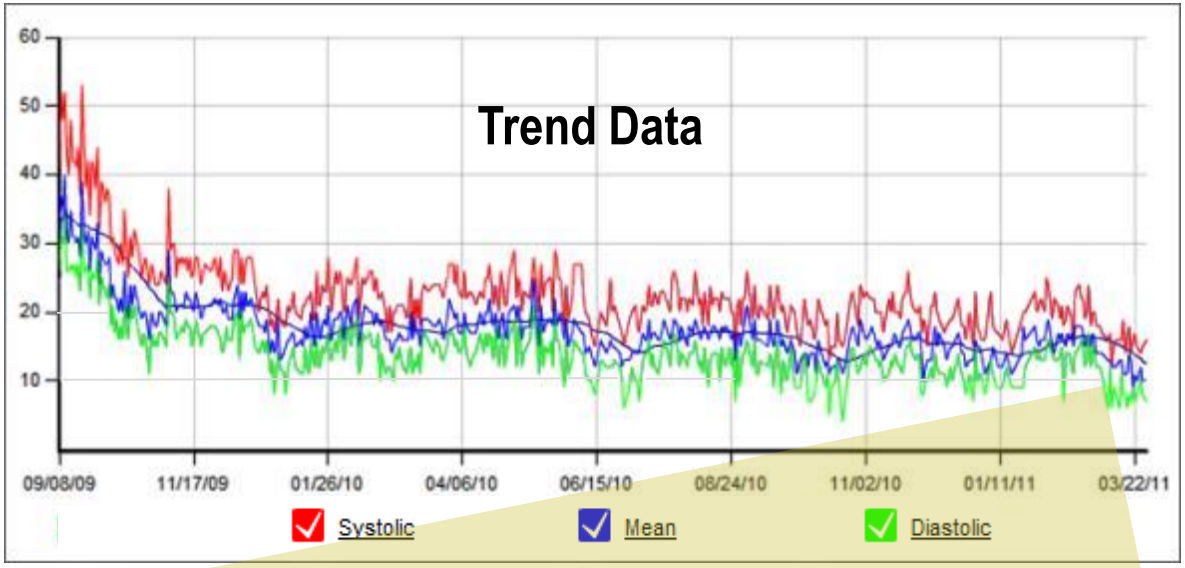
The trials specifically excluded patients with

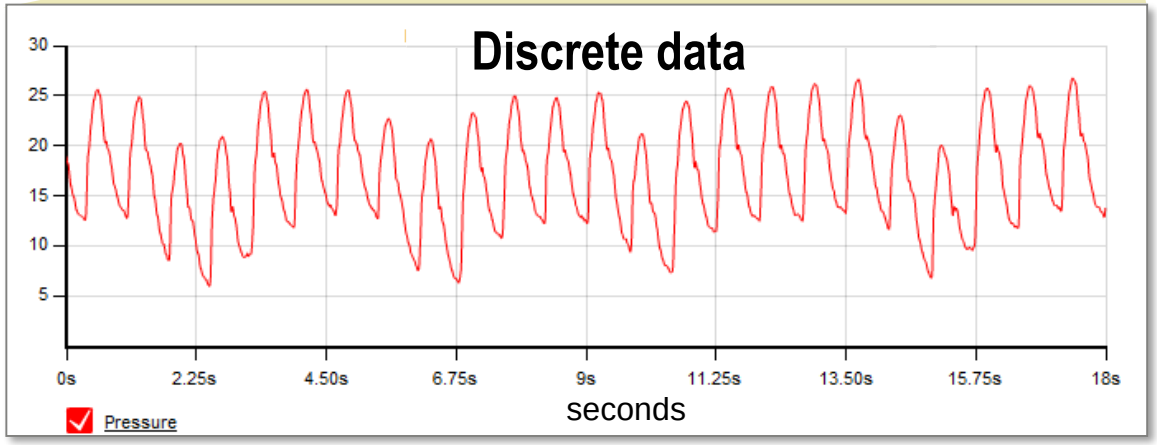
- ACC/AHA stage D heart failure,
- Patients with eGFR less than 25 ml/ kg/1.73m2.
- Patients who were unable to tolerate Plavix and aspirin therapy

Following implantation:

- Patients on warfarin, factor Xa inhibitors or direct thrombin inhibitors were continued following implant of the sensor.
- Otherwise they were instructed to take aspirin 81 or 325 mg daily and clopidogrel 75 mg daily for 1 month after sensor implantation. After 1 month, patients continued with aspirin therapy only.

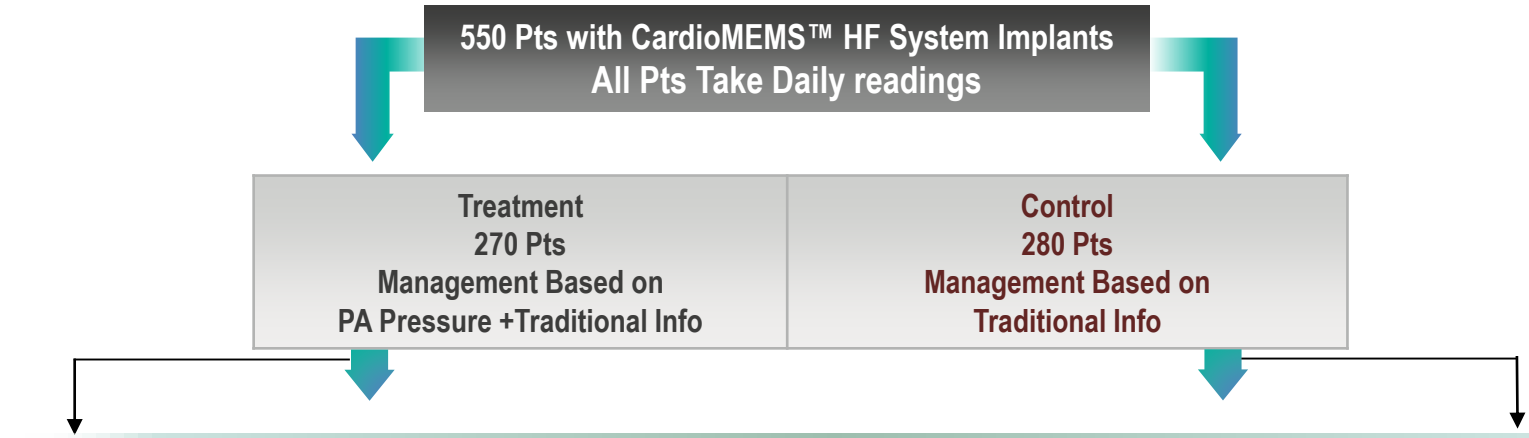
Pulmonary Artery Pressure Database





Reading	
Systolic:	24
Mean:	19
Diastolic:	16
Heart Rate:	81

CHAMPION Clinical Trial: Managing to Target PA Pressures



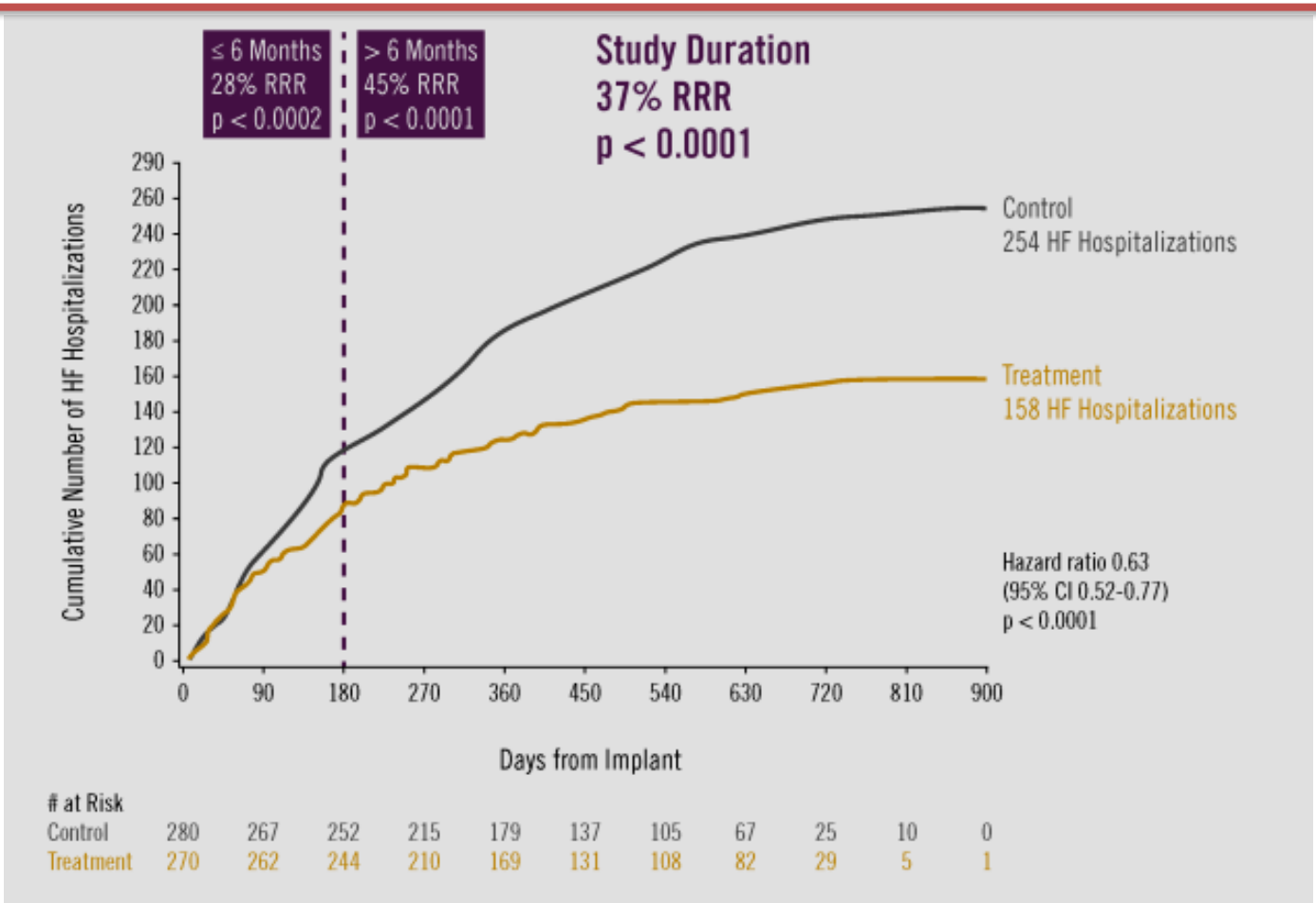
PA pressures were managed to target goal pressures by physicians with appropriate titration of HF medications.

Target Goal PA Pressures:

- PA Pressure Systolic 15 – 35 mmHg
- PA Pressure diastolic 8 – 20 mmHg
- PA Pressure mean 10 – 25 mmHg

Abraham WT, et al. Lancet, 2011.

CHAMPION Clinical Trial: PA Pressure-guided Therapy Reduces HF Hospitalizations

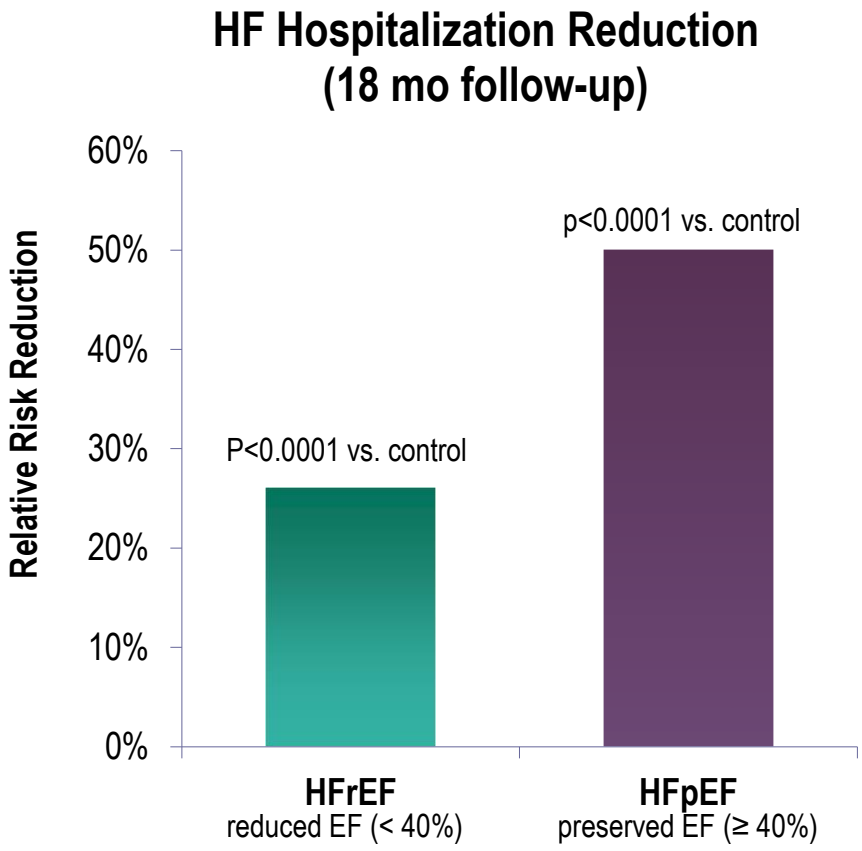


Patients managed with PA pressure data had **significantly fewer HF hospitalizations** as compared to the control group.

Abraham WT, et al. Lancet, 2011.

CHAMPION Clinical Trial: PA Pressure-Guided Therapy Improves Outcomes in Patients with Preserved Ejection Fraction

- Preserved Ejection Fraction Heart Failure (HFpEF) or diastolic HF patients represent ~50% of all HF patients
- Pulmonary artery pressure-guided therapy significantly reduced HF hospitalizations in HFpEF patients in the treatment group by 46% at 6 months ($p<0.0001$) and by 50% at 18 months ($p<0.0001$)
- The effect in HFpEF patients is even more dramatic than HFrEF or systolic patients



Adamson PB,, et al.. Circ Heart Fail. 2014.

CHAMPION Clinical Trial: The Number Needed to Treat (NNT) to Prevent One HF-related Hospitalization is Lower vs. Other Therapies

Intervention	Trial	Mean Duration of Randomized Follow-Up	Annualized Reduction in HF Hospitalization Rates	NNT per year to Prevent 1 HF Hospitalization
Beta-blocker	COPERNICUS	10 months	33%	7
Aldosterone antagonist	RALES	24 months	36%	7
CRT	CARE-HF	29 months	52%	7
Beta-blocker	MERIT-HF	12 months	29%	15
ACE inhibitor	SOLVD	41 months	30%	15
Aldosterone antagonist	EMPHASIS-HF	21 months	38%	16
Digoxin	DIG	37 months	24%	17
Angiotensin receptor blocker	Val-HeFT	23 months	23%	18
Angiotensin receptor blocker	CHARM	40 months	27%	19
PA pressure monitoring	**CHAMPION**	**17 months**	**33%**	**4**

The CardioMEMS HF System has shown:

- 33% overall reduction in heart failure hospitalizations over an average of 18 months
- 50% reduction in heart failure hospitalization for HFpEF patients over an average of 18 months
- Shorter length or stay when patients are hospitalized
- 98.6% freedom from device or system related complications
- Better patient quality of life as shown by significant improvements in Minnesota Living with Heart Failure Questionnaire scores

Device related Complications

- In CHAMPION Trial total device or system related complication was 1% with only one case of PA injury was identified in the 550-patients.
- However the MAUDE database for adverse events reported between May 28, 2014—the date of FDA approval—and May 28, 2017, finding 155 reports involving 177 events.

Device related Complications

Adverse events included:

- Sensor failure, malfunction,
- Migration requiring recalibrations, reimplantations, and hospitalizations
- PA injury/hemoptysis
- Deaths, related to PA injury/hemoptysis
- Technical challenges with implantation
- Access site-related bleeding or infection
- Pulmonary embolism or device thrombosis

Take Home Message

- HF continues to be a major public health problem with a significant financial burden on the economy.
- With longer life expectancy, more reliable and valid methods will be required to appropriately intervene in and prevent HF-related hospitalization and death.
- Implantable hemodynamic devices are the newly emerging tools in the field of HF management.
- CardioMEMS™ appears to be a significant technologic breakthrough
- Larger multicenter trials are required to make valid recommendations