Monitoring Heart Failure: Implantable Devices to Guide Management

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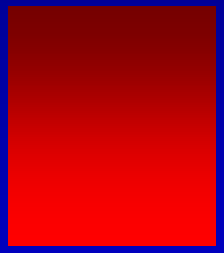
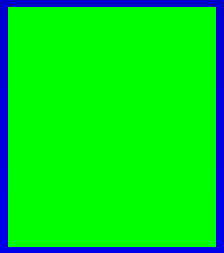
Volume Management in Heart Failure

- Elevated intra-cardiac and pulmonary artery pressures define the clinical syndrome of “congestive” heart failure
- Increasing pressures result in worsening symptoms and increased risk of hospitalization
- Current tools are not adequate for the day-to-day management of volume status or intra-cardiac and pulmonary artery pressures

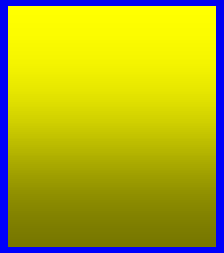
Key Therapeutic Goal in Heart Failure: Maintain Optimal Volume/Pressure Status



Hypervolemia/Elevated Intra-cardiac and Pulmonary Artery Pressures:
Increased symptoms, increased risk of hospitalization, increased risk of arrhythmias, increased mortality



Optivolemia/Normal Intra-cardiac and Pulmonary Artery Pressures:
Low risk



Hypovolemia/Low Intra-cardiac and Pulmonary Artery Pressures:
Symptomatic hypotension, syncope, pre-renal azotemia

Limitations of Available Monitoring Systems

- Weight and Symptoms – Recent large, landmark clinical studies (Tele-HF, TIM-HF) investigating the effectiveness of telemonitoring demonstrated no benefit in reducing HF hospitalizations
- BNP - PRIMA Study guided identification of patients at risk for HF events, but showed no significant reduction in HF-related admissions
- Device-Based Diagnostics - May be useful for identifying patients that may be at higher risk for a HF hospitalization(PARTNERS-HF Study), but of limited utility in day-to-day HF management

Tele-HF: Yale Heart Failure Telemonitoring Study; NEJM, 2010
TIM-HF: Telemonitoring Intervention in Heart Failure, Eur J. Heart Failure, 2010
PRIMA: Can Pro-BNP guided heart failure therapy improve morbidity and mortality? J Am Coll Card, 2010
PARTNERS-HF: Combined Heart Failure Device Diagnostics Identify Patients at Higher Risck of Subsequent Heart Failure Hospitalizations. J Am Coll Card, 2010

Implantable Hemodynamic Monitors

LV Pressure Sensor

RV Pressure Sensors

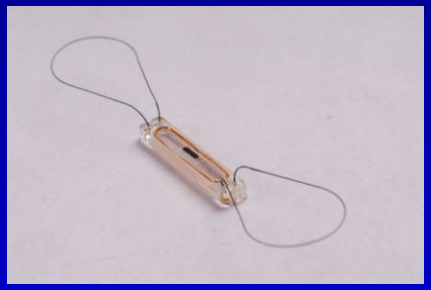
PA Pressure Sensors

LA Pressure Sensor

The Pulmonary Artery Pressure Measurement System*

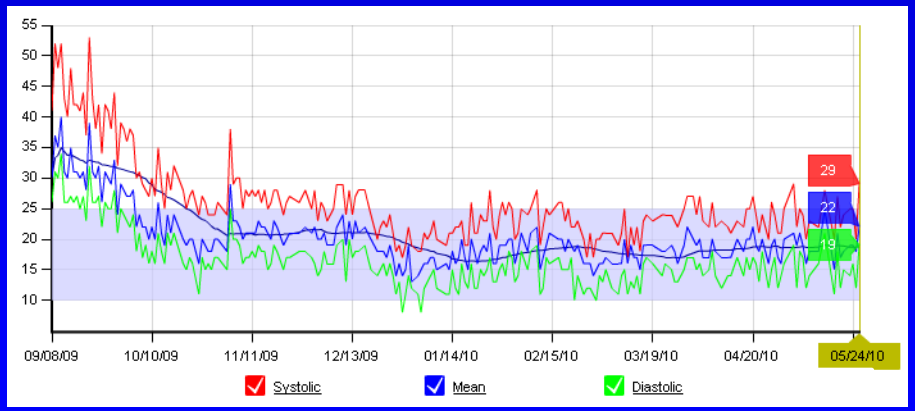
Catheter-based delivery system

MEMS-based pressure sensor



Home electronics

PA Measurement database



*CardioMEMS Inc., Atlanta, Georgia, USA

Primary Results of the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) Trial

Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

*William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynn Warner Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group**

Summary

Background Results of previous studies support the hypothesis that implantable haemodynamic monitoring systems might reduce rates of hospital admission in patients with heart failure. We undertook a single-blind trial to assess this approach.

Methods Patients with New York Heart Association (NYHA) class III heart failure, irrespective of the ejection fraction, and a previous hospital admission for heart failure were enrolled in 64 centres in the USA. They were randomly assigned by use of a centralised electronic system and assigned to management with a wireless implantable

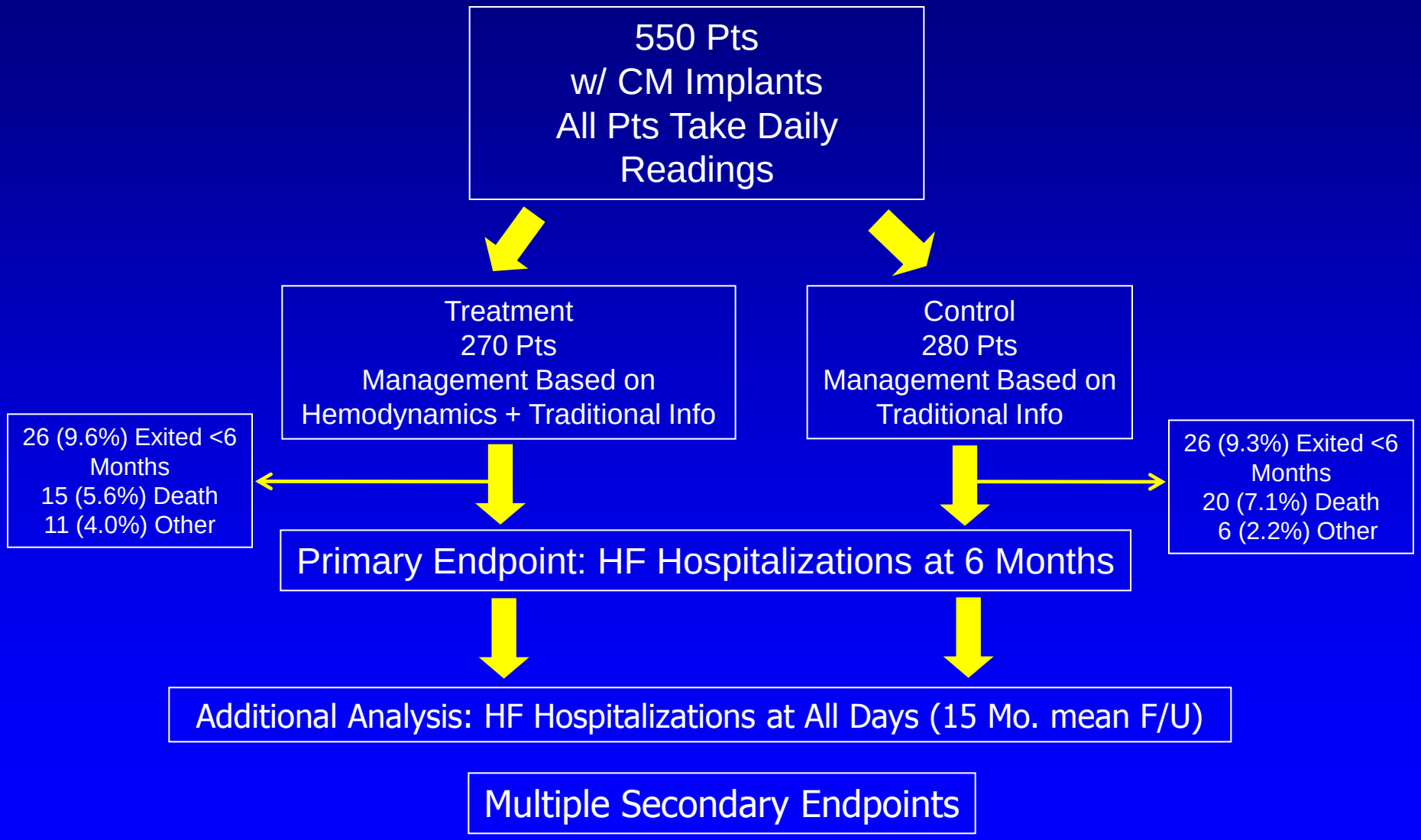
Lancet 2011; 377:

Published Online February 10, 2011

CHAMPION Study Design

- Prospective, multi-center, randomized (1:1), controlled single-blind clinical trial
  - Treatment group received traditional HF management guided by hemodynamic information from the sensor
  - Control group received traditional HF disease management
- 550 subjects enrolled at 63 sites in the U.S. between October 2007 and September 2009
- All subjects followed in their randomized single-blind study assignment until the last patient reached 6 months of follow-up

CHAMPION Patient Disposition



Primary Safety Results

	Consented Not Enrolled (n=25)	Treatment (n=270)	Control (n=280)	All Patients	p-Value
Primary Safety Endpoint: Device/System Related Complications at 6 Months # (%)	**2(8)**	**3 (1.1)**	**3 (1.1)**	**8 (1.4)**	**<0.0001[1]**
Primary Safety Endpoint: Pressure Sensor Failures at 6 Months # (%)	**0 (0)**	**0 (0)**	**0 (0)**	**0 (0)**	**< 0.0001[2]**

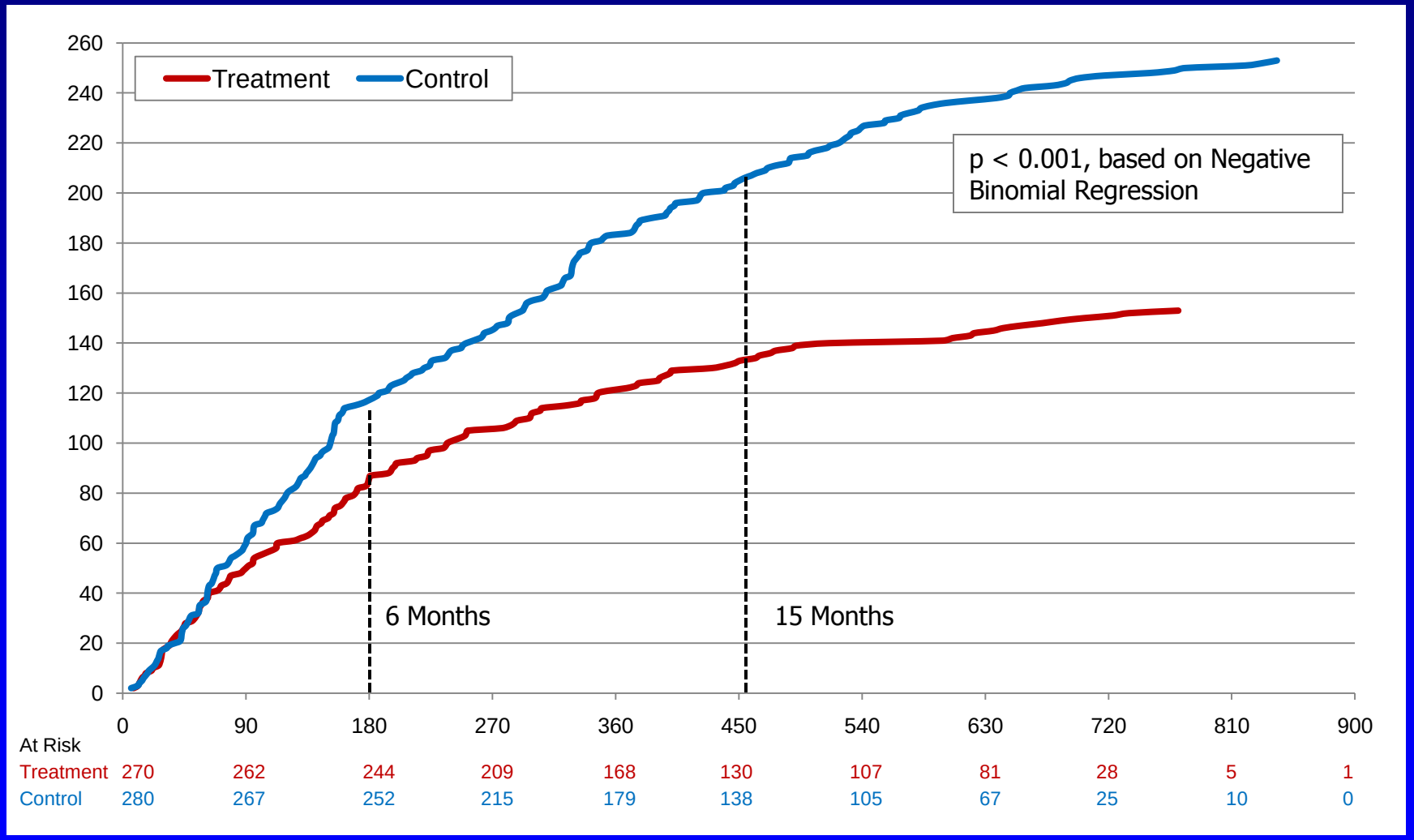
[1]p-value from exact test of binomial proportions compared to 80% for All Patients
[2]p-value from exact test of binomial proportions compared to 90% for All Patients

Primary Efficacy Results

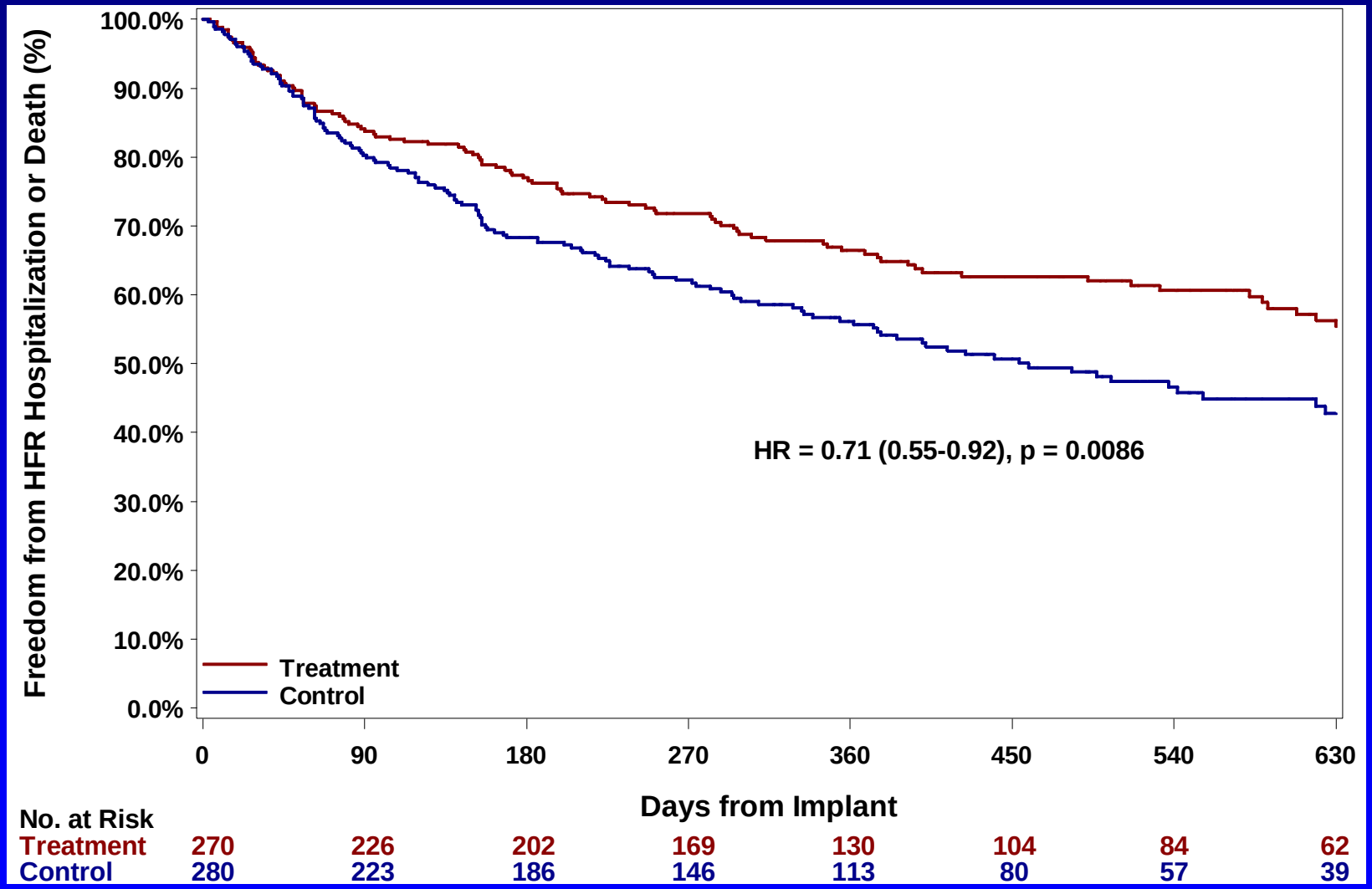
	Treatment (n=270)	Control (n=280)	Relative Risk Reduction	p-Value[1]	NNT
Primary Efficacy Endpoint: HF Related Hospitalizations Up To 6 Months # (Rate)	**83 (0.31)**	**120 (0.44)**	**30%**	**<0.0001**	**8**
Ancillary Analysis: HF Related Hospitalizations Over Entire Randomized Period # (Annualized Rate) [Mean F/U: 455±211 (1–931)]	**153 (0.44)**	**253 (0.72)**	**39%**	**<0.0001**	**4**

[1]p-value from negative binomial regression
NNT = Number Needed to Treat

Cumulative HF Hospitalizations Over Entire Randomized Follow-Up Period



Freedom From First HF Hospitalization or Death



No Adverse Impact on Non-HF Hospitalizations

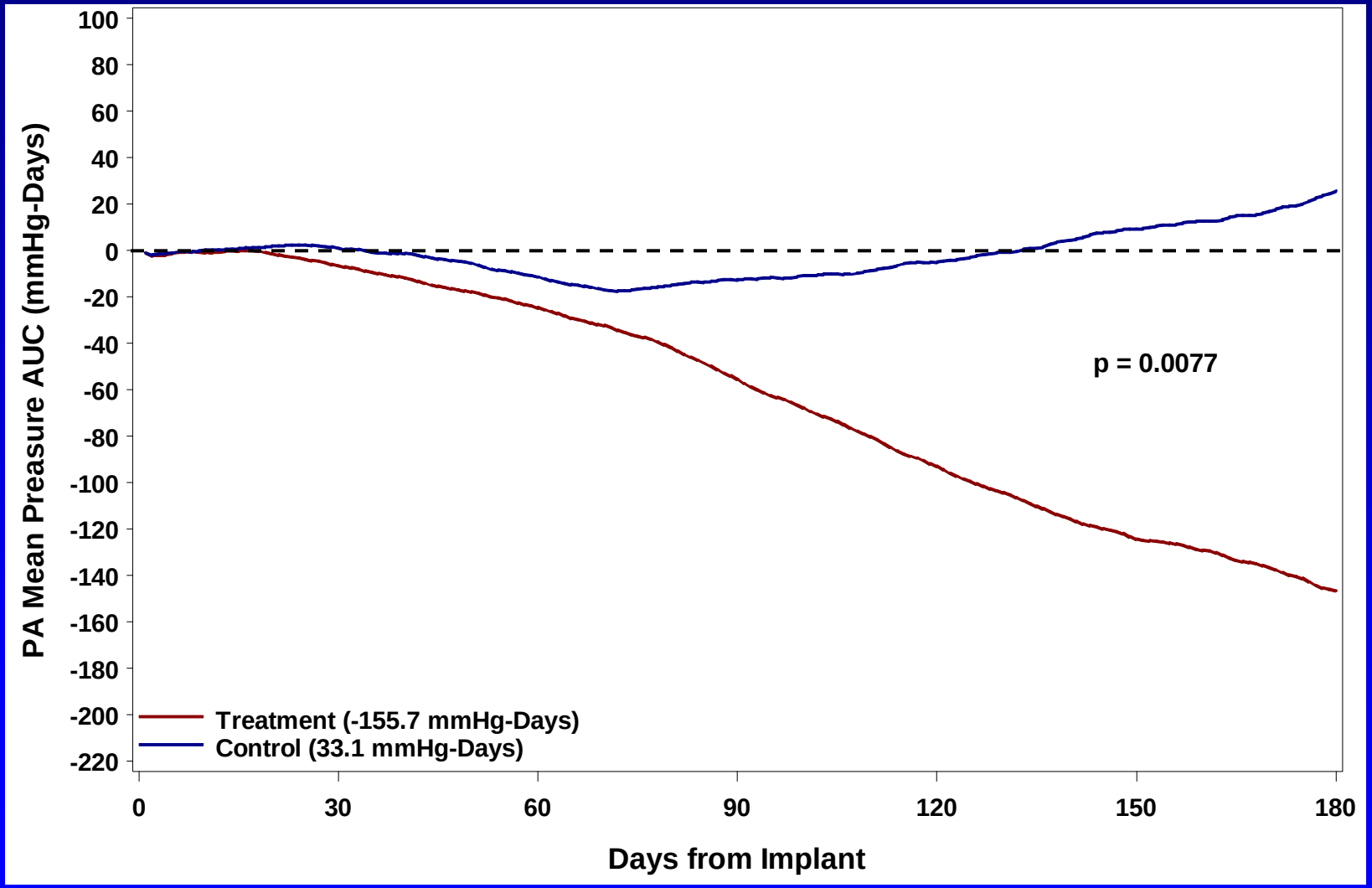
Hemodynamic monitoring reduced heart failure related hospitalizations without increasing non-heart failure hospitalizations

	Treatment	Control
6 Months		
All Cause Hospitalizations	229	263
- HFR	83	120
Non-HF Hospitalizations	**146**	**143**
All Days		
All Cause Hospitalizations	484	590
- HFR	153	253
Non-HF Hospitalizations	**331**	**337**

Secondary Efficacy Results

	Treatment (n=270)	Control (n=280)	p-Value
Change from Baseline in Mean Pulmonary Artery Pressure at 6 Months Mean AUC	**-156**	**33**	**0.008**
Subjects Hospitalized for Heart Failure at 6 Months # (%)	**54 (20)**	**80 (29)**	**0.022**
Days Alive Outside Hospital at 6 Months Mean	**174.4**	**172.1**	**0.022**
Minnesota Living with Heart Failure Questionnaire at 6 Months Mean	**45**	**51**	**0.024**

AUC PA Mean Change from Baseline up to 6 Months



Heart Failure Medication Changes at 6 Months

	baseline medications		medication changes up to 6 months			
	Patients		Patients		Medications	
	Treatment (270)	Control (280)	Treatment (270)	Control (280)	Treatment (2493)	Control (1076)
ARB	42 (15.6%)	59 (21.1%)	32 (11.9%)	25 (8.9%)	144	0.0003
Ace Inhibitors	170 (63.0%)	173 (61.8%)	98 (36.3%)	65 (23.2%)	68	0.0290
Aldosterone Antagonist	117 (43.3%)	115 (41.1%)	72 (26.7%)	51 (18.2%)	160	0.0027
Beta Blocker	243 (90.0%)	261 (93.2%)	122 (45.2%)	97 (34.6%)	498	<0.0001
Diuretic-Loop	250 (92.6%)	264 (94.3%)	213 (78.9%)	163 (58.2%)	87	<0.0001
Diuretic-Thiazide	48 (17.8%)	51 (18.2%)	94 (34.8%)	57 (20.4%)	51	0.0022
Hydralazine	36 (13.3%)	33 (11.8%)	55 (20.4%)	30 (10.7%)	53	<0.0001
Nitrate	66 (24.4%)	57 (20.4%)	103 (38.1%)	35 (12.5%)	1061	<0.0001
Total	267	280	253	225	2493	1076
HF Medication Changes Mean±StdDev (N)					9.2±7.5 (270)	3.8±4.5 (280)
Median	N/A	N/A	N/A	N/A	7.0	3.0
(Min, Max)					(0.0, 35.0)	(0.0, 38.0)
					P < 0.0001	

5.4 incremental medication changes

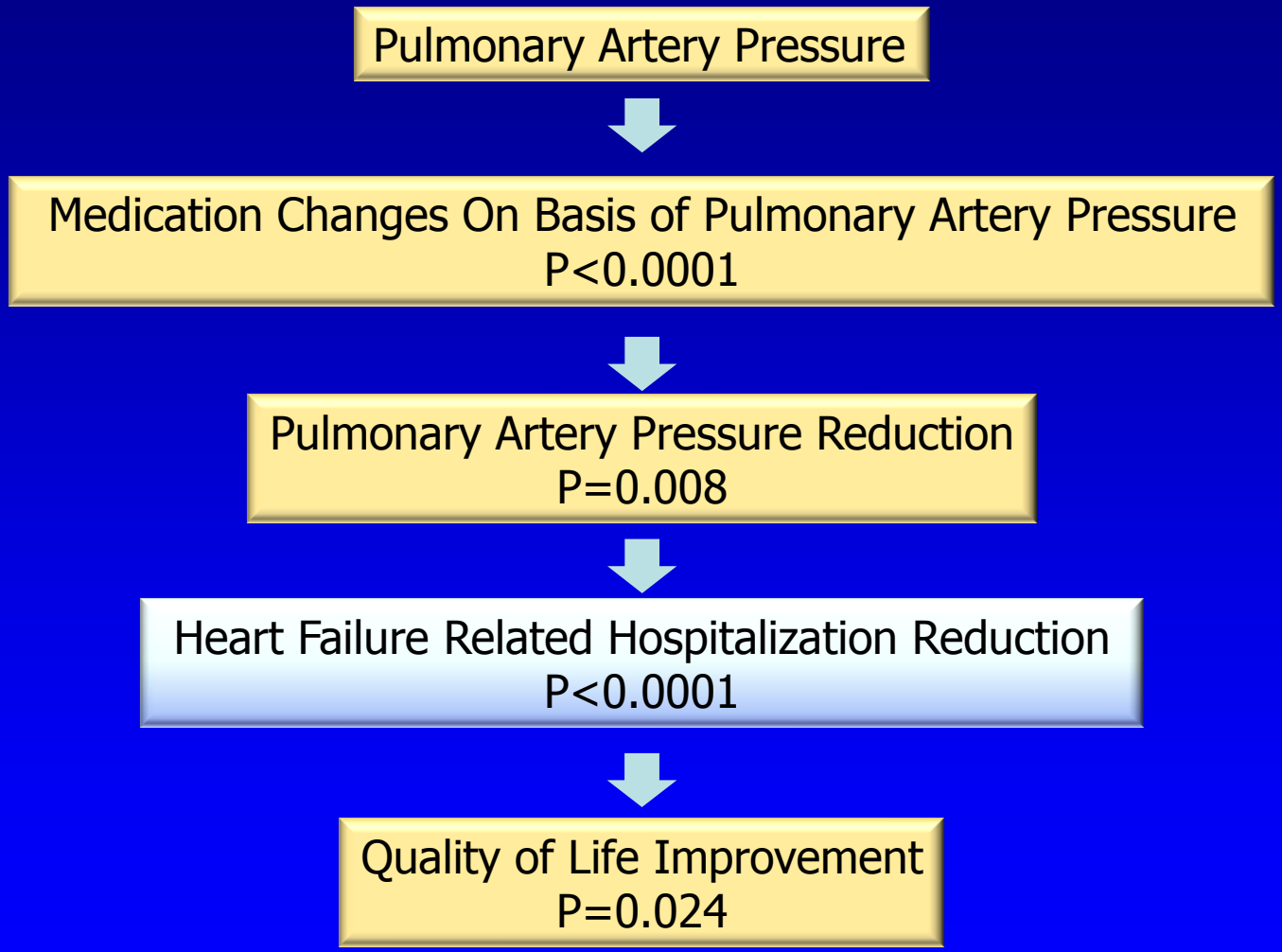
Efficacy Analysis by Baseline Ejection Fraction

	Treatment (270)			Control (280)			All Patients (550)
	# Pts. (n)	# Hosp. (n)	Hosp. Rate (events/ patient-yr)	# Pts. (n)	# Hosp. (n)	Hosp. Rate (events/ patient-yr)	p-value [1]
EF < 40%	208	73	0.36	222	101	0.47	0.0074
EF ≥ 40%	62	10	0.16	57	19	0.33	<0.0001

[1] P-value from the negative binomial regression (NBR) model.

- These results demonstrate that HF management based on PAP is effective in reducing HFR hospitalizations in patients with either reduced or preserved LV function
- This trial represents one of the first successful management strategies to reduce hospitalization risks for heart failure patients with preserved ejection fraction

CHAMPION: Putting It Altogether



P values for Treatment Vs Control Group

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Physician-Directed Patient Self-Management of Left Atrial Pressure in Advanced Chronic Heart Failure

Jay Ritzema, Richard Troughton, Iain Melton, Ian Crozier, Robert Doughty, Henry Krum, Anthony Walton, Philip Adamson, Saibal Kar, Prediman K. Shah, Mark Richards, Neal L. Eigler, James S. Whiting, Garrie J. Haas, J. Thomas Heywood, Christopher M. Frampton, William T. Abraham and on Behalf of the Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients (HOMEOSTASIS) Study Group

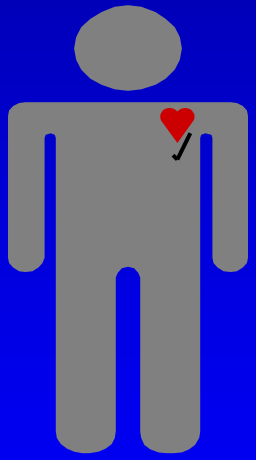
Circulation published online Feb 22, 2010;

Circulation 2010; 121:1086-1095

Physician-Directed, Patient Self-Management Using the LAP Monitoring System

Patient obtains LAP readings twice a day with PAM at rest & supine prior to meds

LAP data uploaded to Clinician's PC Software



Objective = Control LAP Excursions

Patient uses DynamicRx to self-titrate HF meds

Clinician formulates DynamicRX based on LAP data

HOMEOSTASIS I & II

Endpoints, Design, Subject Accounting

Open-label, registry

1º Endpoint (*safety*)

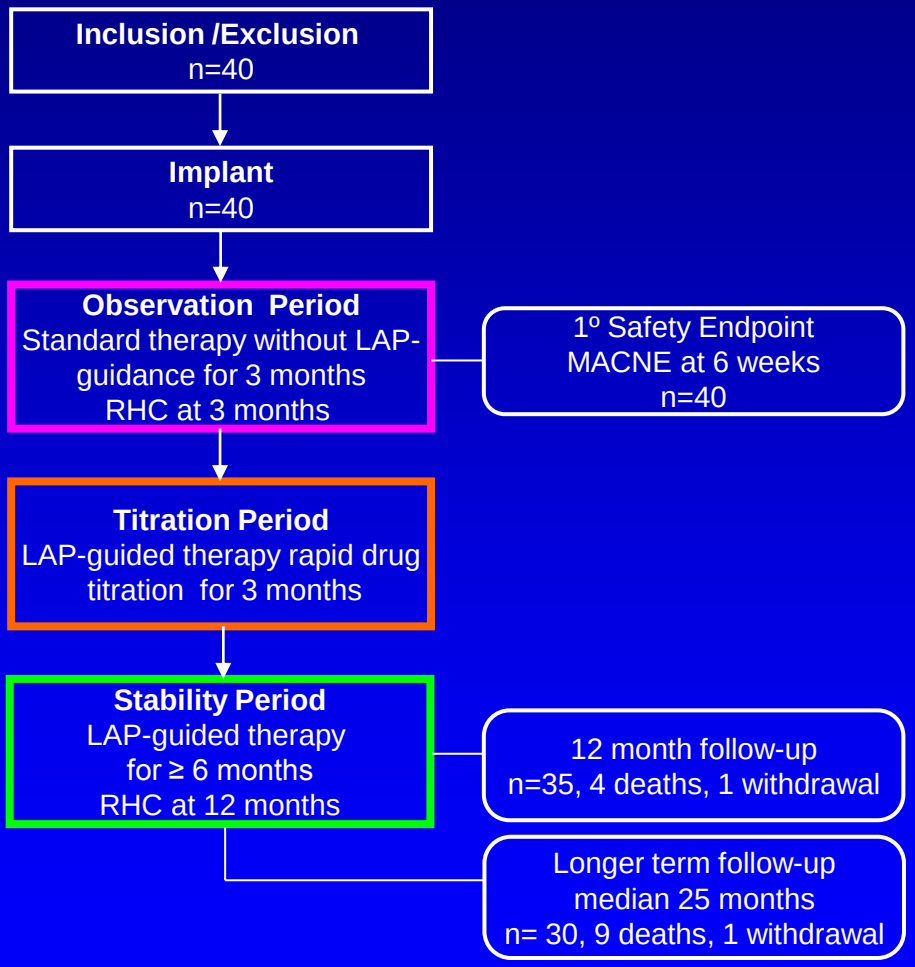
- Freedom from Major Adverse Cardiac and Neurological Events (MACNE) at 6 weeks

2º Endpoints (*functionality*)

- Calibration
- LAP vs. PCWP

3º Endpoints (*Effectiveness surrogates*)

- Control of LAP
- Hospitalization
- Clinical parameters



Ritzema J, et al. Physician-Directed Patient Self-Management of Left Atrial Pressure in Advanced Heart Failure. Circulation 2010;121:1086-1095.

HF Event Rates (ADHF and All-Cause Death)

Comparison of Periods with and without LAP-Guidance

Period	Annualized Event Rate	P-values	
12-mo period before enrollment	1.4 (1.1-1.9)	0.054	
First 3 mo Observation Period	0.68 (0.33-1.4)	0.041	<0.001
After mo 3 Titration/Stability Periods	0.28 (0.18-0.45)		

Ritzema J, et al. Physician-Directed Patient Self-Management of Left Atrial Pressure in Advanced Heart Failure. Circulation 2010;121:1086-1095.