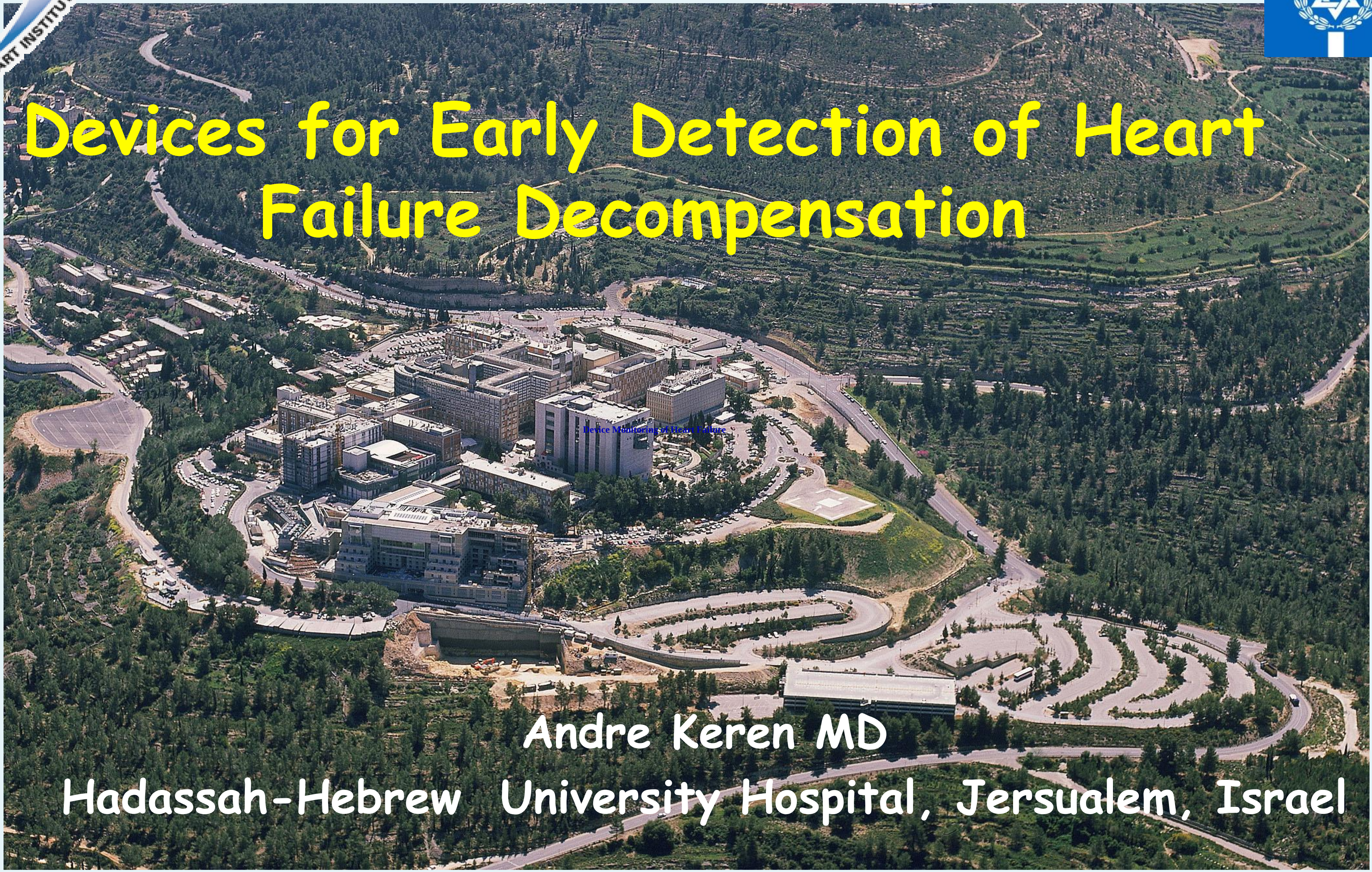
Devices for Early Detection of Heart Failure Decompensation



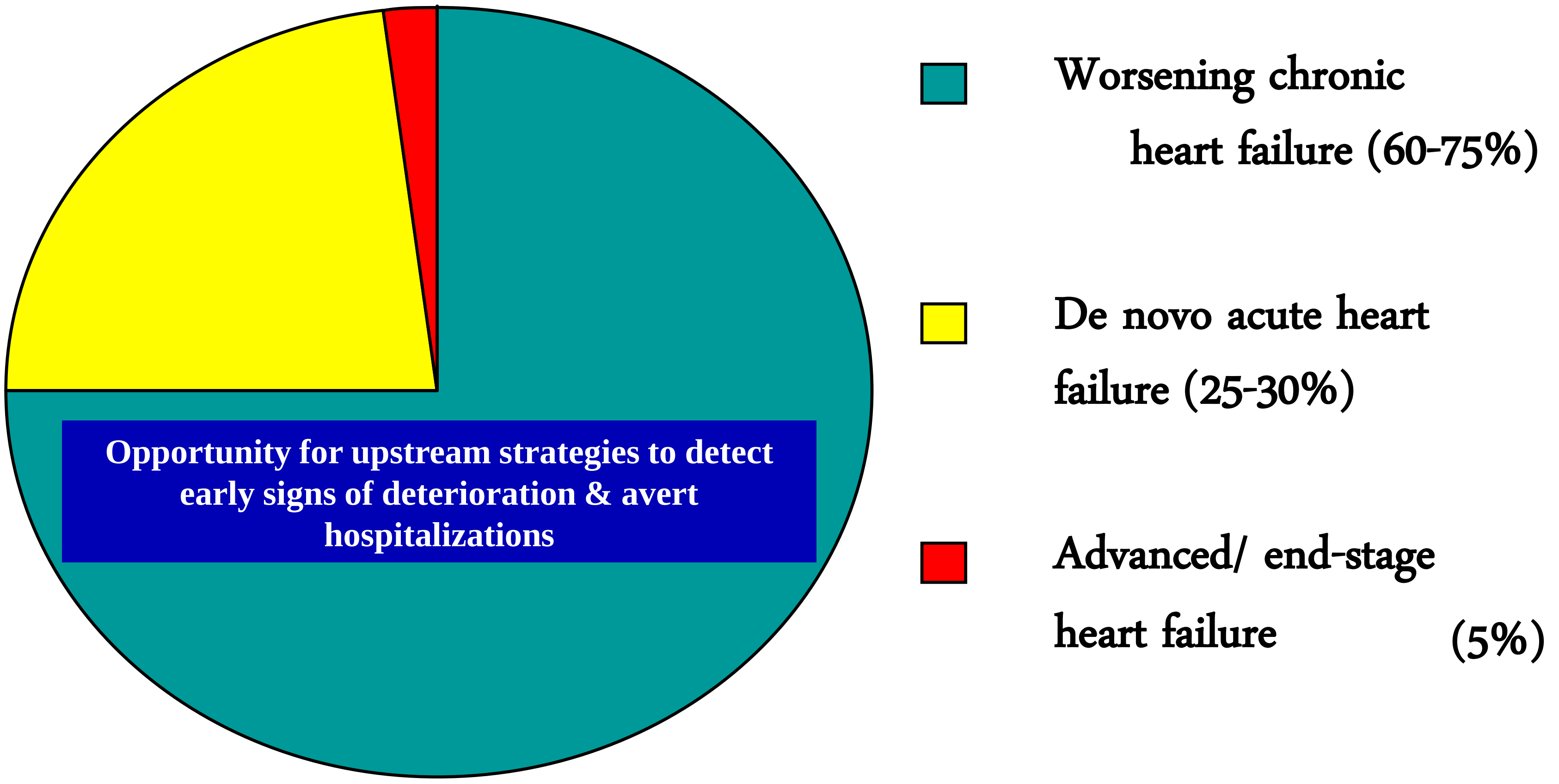
Andre Keren MD

Hadassah-Hebrew University Hospital, Jersualem, Israel

20.3.2014

Disclosure: Consultant for CardioLogic Innovations

Worsening Chronic Heart Failure: The Major Reason for Heart Failure Hospitalizations

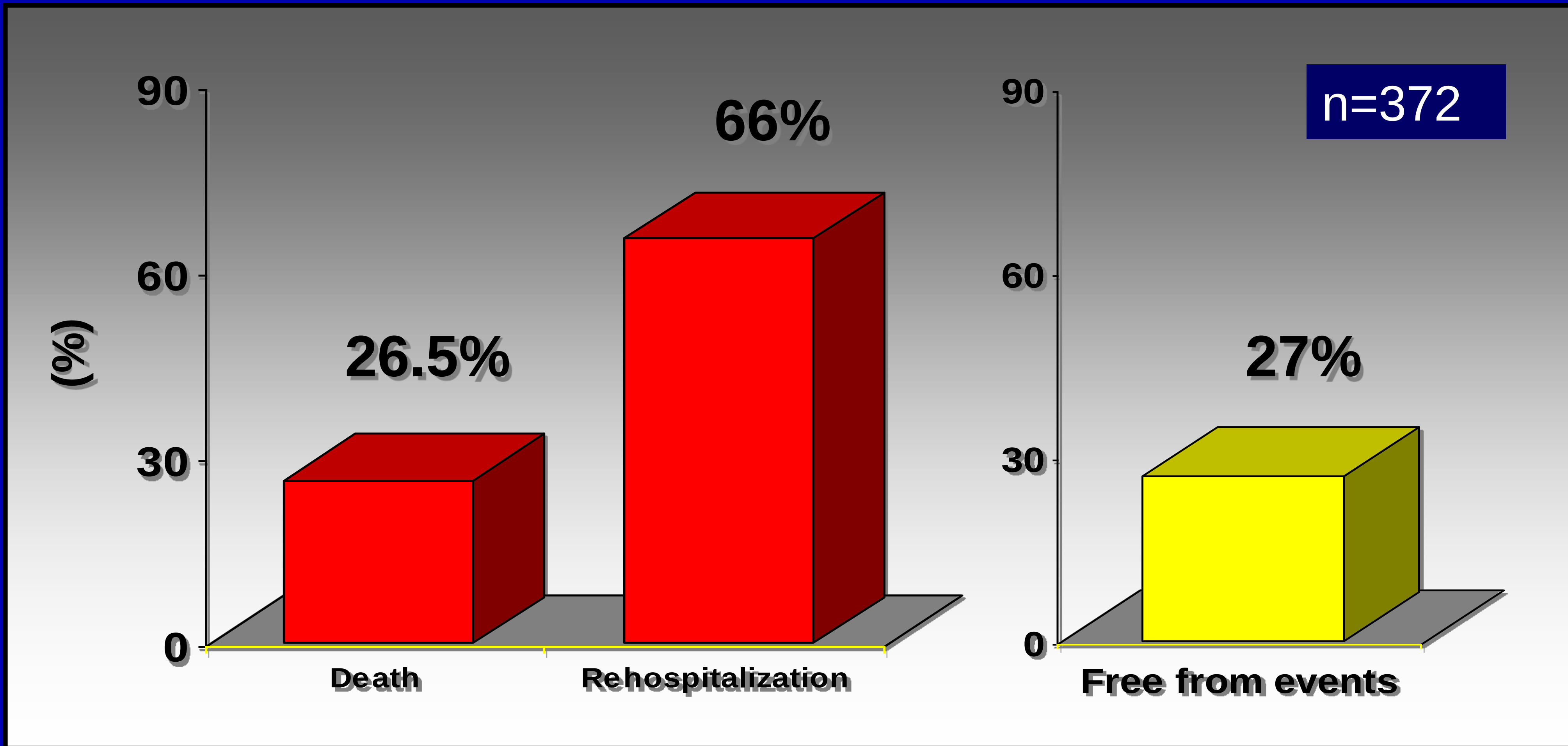


Despite optimal medical therapy plus CRT - high mortality rates and readmission with heart failure

Fonarow GC. Rev Cardiovasc Med. 2003; 4 (Suppl. 7): 21 (ADHERE)

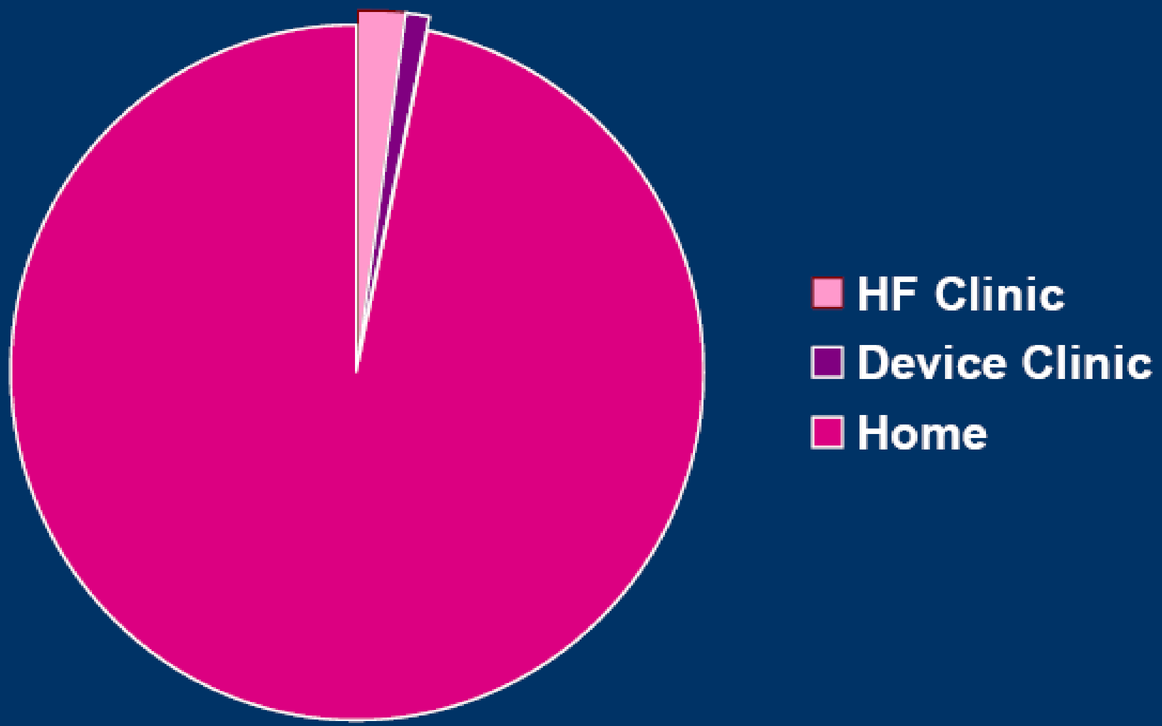
Cleland JG et al. Eur Heart J. 2003; 24: 442 (Euro Heart Failure Survey)

One Year Clinical Event Rate in Heart Failure in Hadassah, Jerusalem



Gotsman I, et al 2008

Most Days of Heart Failure Management Are Not Clinic Days



Stevenson LE, ESC Congress, Paris, 2011

Complex telemonitoring or a simple phone call, which is more effective in post-discharge heart failure management?

Monitoring technology	All-cause mortality, HR (95% CI), p	All-cause hospitalization, HR (95% CI), p	HF hospitalization, HR (95% CI), p
Telephone call	0.86 (0.75-1.00), 0.04	0.91 (0.84-0.97), 0.008	0.77 (0.68-0.87), <0.0001
Interactive voice recognition	0.70 (0.24-2.11), 0.53	1.18 (0.83-1.66), 0.35	1.03 (0.60-1.78), 0.91
"Complex" telemonitoring	0.63 (0.51-0.77), <0.0001	0.91 (0.84-0.99), 0.02	0.79 (0.67-0.94), 0.008

Clark RA, Inglis SC, McAllister FA, et al. Heart Failure Society of America 2011 Scientific Meeting; September 18-21, 2011; Boston, MA.

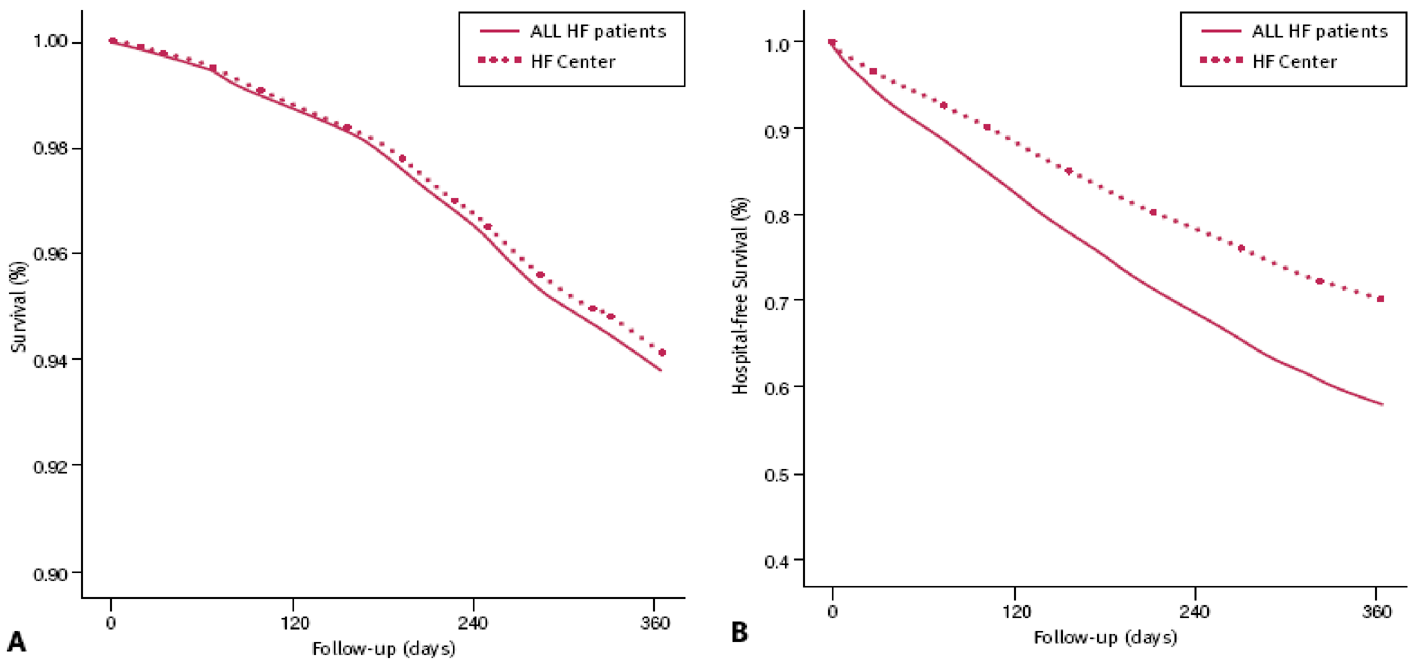
IMAJ • VOL 13 • AUGUST 2011

Clinical Outcome of Patients with Chronic Heart Failure Followed in a Specialized Heart Failure Center

Israel Gotsman MD[1,2], Donna Zwas MD[1,2], Zehava Zemora RN[2], Refat Jabara MD[1,2], Dan Admon MD[1], Chaim Lotan MD[1] and Andre Keren MD[1,2]

[1]Heart Institute, Hadassah University Hospital, Jerusalem, Israel
[2]Heart Failure Center, Clalit Health Services, Jerusalem, Israel

Figure 1. Adjusted survival rate **[A]** and cardiac-related hospitalization rate **[B]** of patients treated in the HF center versus all HF patients by Cox regression analysis. There was no significant difference in survival between the groups: hazard ratio 0.93, 95% confidence interval 0.60–1.45, $P = 0.7$. There was a significant reduction in hospitalization rate in patients treated in the HF center: HR 0.65, 95% CI 0.53–0.80, $P < 0.0001$



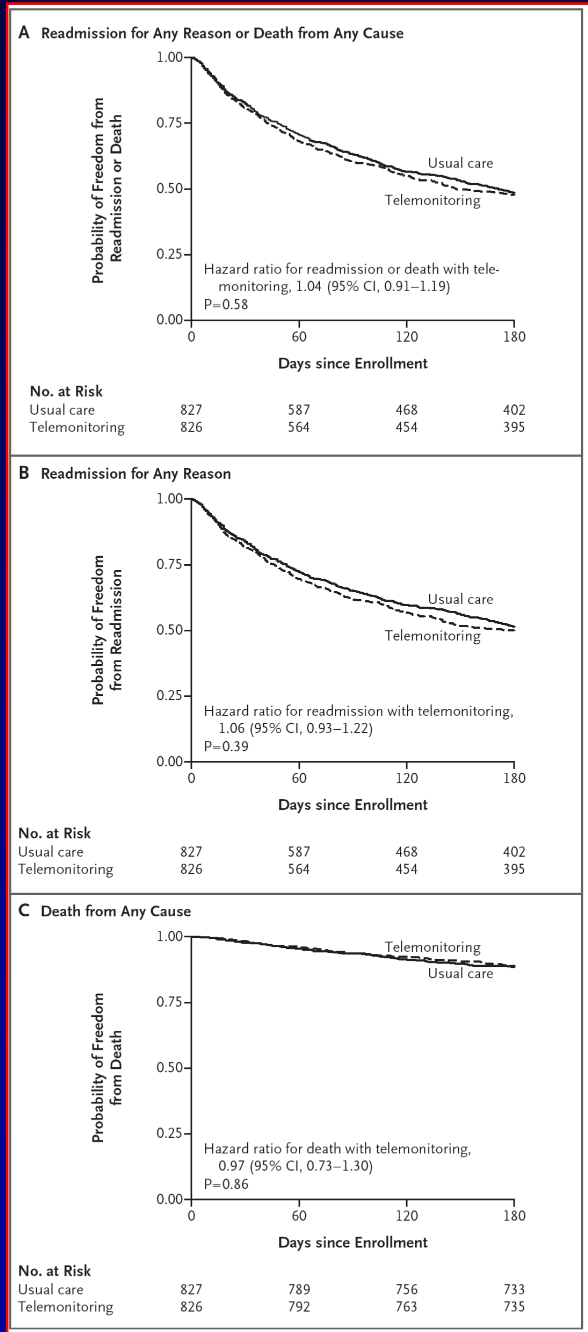
Remote Monitoring Approaches

- **Symptoms, Blood Pressure, Weight**
- **Implanted Device (CRT, ICD) Based Parameters (Intrathoracic Impedance)**
- **Implanted Hemodynamic Monitors**

- Noninvasive Assessment of Congestion
- Biomarkers

Studies Based on Clinical Parameters

Symptoms, Weight, Blood pressure



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Telemonitoring in Patients with Heart Failure

Sarwat I. Chaudhry, M.D., Jennifer A. Mattera, M.P.H., Jeptha P. Curtis, M.D., John A. Spertus, M.D., M.P.H., Jeph Herrin, Ph.D., Zhenqiu Lin, Ph.D., Christopher O. Phillips, M.D., M.P.H., Beth V. Hodshon, M.P.H., J.D., R.N., Lawton S. Cooper, M.D., M.P.H., and Harlan M. Krumholz, M.D.

N Engl J Med 2010;363:230-2309

TELE-HF STUDY

Telephone-based Interactive Voice Response System

Included 1653 pts recently hospitalized for HF

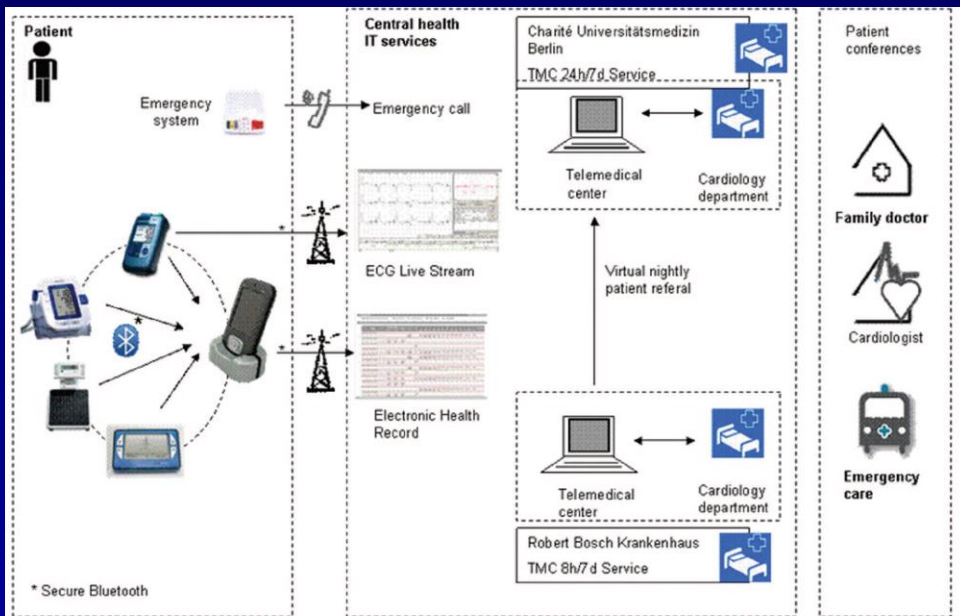
Daily information on symptoms, weight

Result: No difference in Deaths, Readmissions or Combined Parameter

Impact of Remote Telemedical Management on Mortality and Hospitalizations in Ambulatory Patients With Chronic Heart Failure

The Telemedical Interventional Monitoring in Heart Failure Study

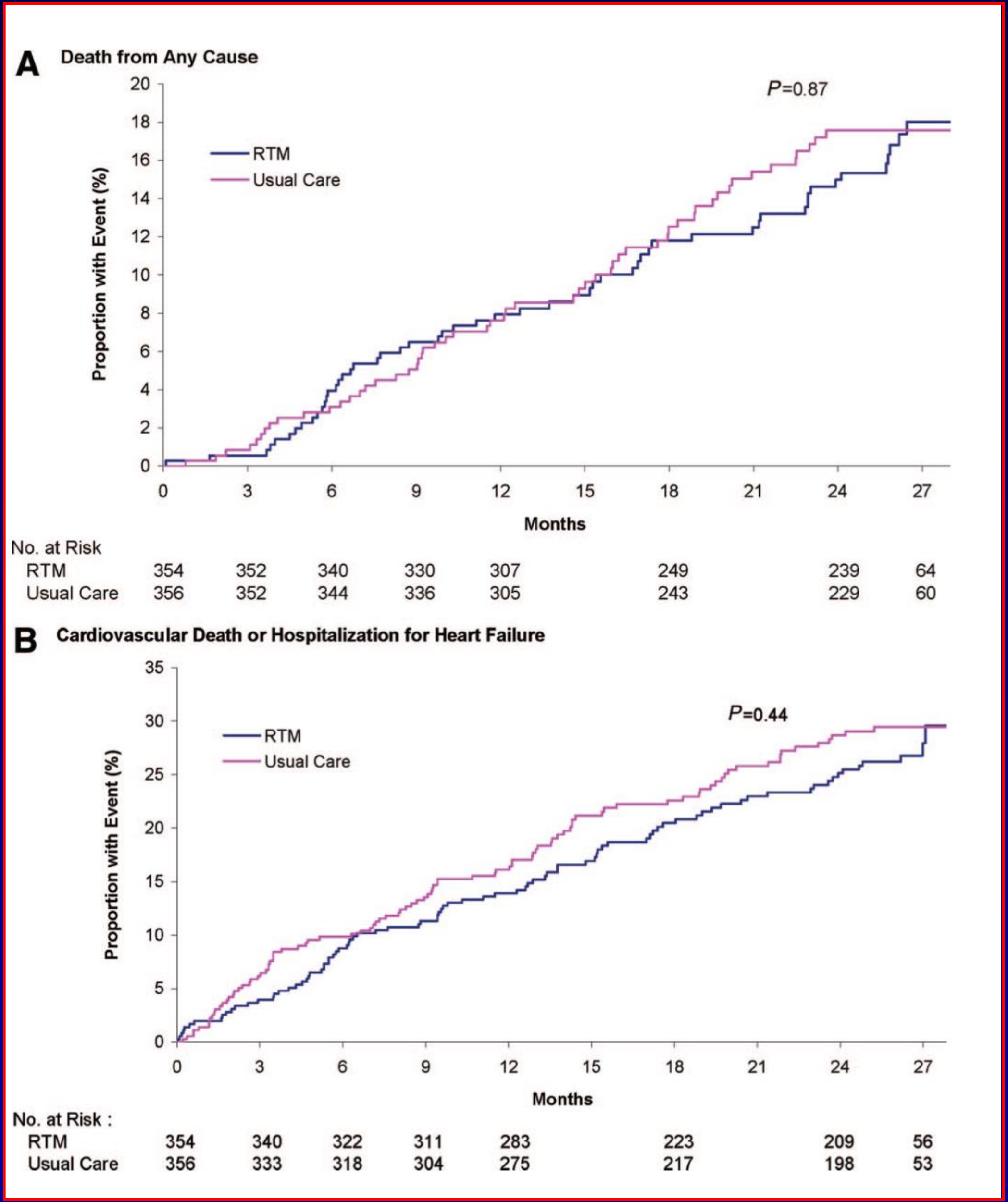
Friedrich Koehler, MD; Sebastian Winkler, MD; Michael Schieber, MD; Udo Sechtem, MD; Karl Stangl, MD; Michael Böhm, MD; Herbert Boll, MD; Gert Baumann, MD; Marcus Honold, MD; Kerstin Koehler, MD; Goetz Gelbrich, PhD; Bridget-Anne Kirwan, PhD; Stefan D. Anker, MD, PhD; on behalf of the Telemedical Interventional Monitoring in Heart Failure Investigators



TIM-HF Study

- LVEF<35%+ HF hospitalization or LVEF<25%
- 710 pts with stable CHF, NYHA II/III
- Data collected: symptoms, weight, BP, ECG
- Automatically transmitted to telemedical center
- Median follow up 26 months

Koehler F, Circulation 2011;123:1873-1880



TIM-HF Study

Remote Telemedical Management had no effect on all cause mortality, cardiovascular death or hospitalization for HF

Koehler F, Circulation 2011;123:1873-1880

Table I Diagnostic value of clinical markers of congestion

Sign or symptom	Sensitivity	Specificity	PPV	NPV
Dyspnoea on exertion	66	52	45	27
Orthopnoea	66	47	61	37
Oedema	46	73	79	46
Resting JVD	70	79	85	62
S3	73	42	66	44
Chest X-ray				
Cardiomegaly	97	10	61	—
Redistribution	60	68	75	52
Interstitial oedema	60	73	78	53
Pleural effusion	43	79	76	47

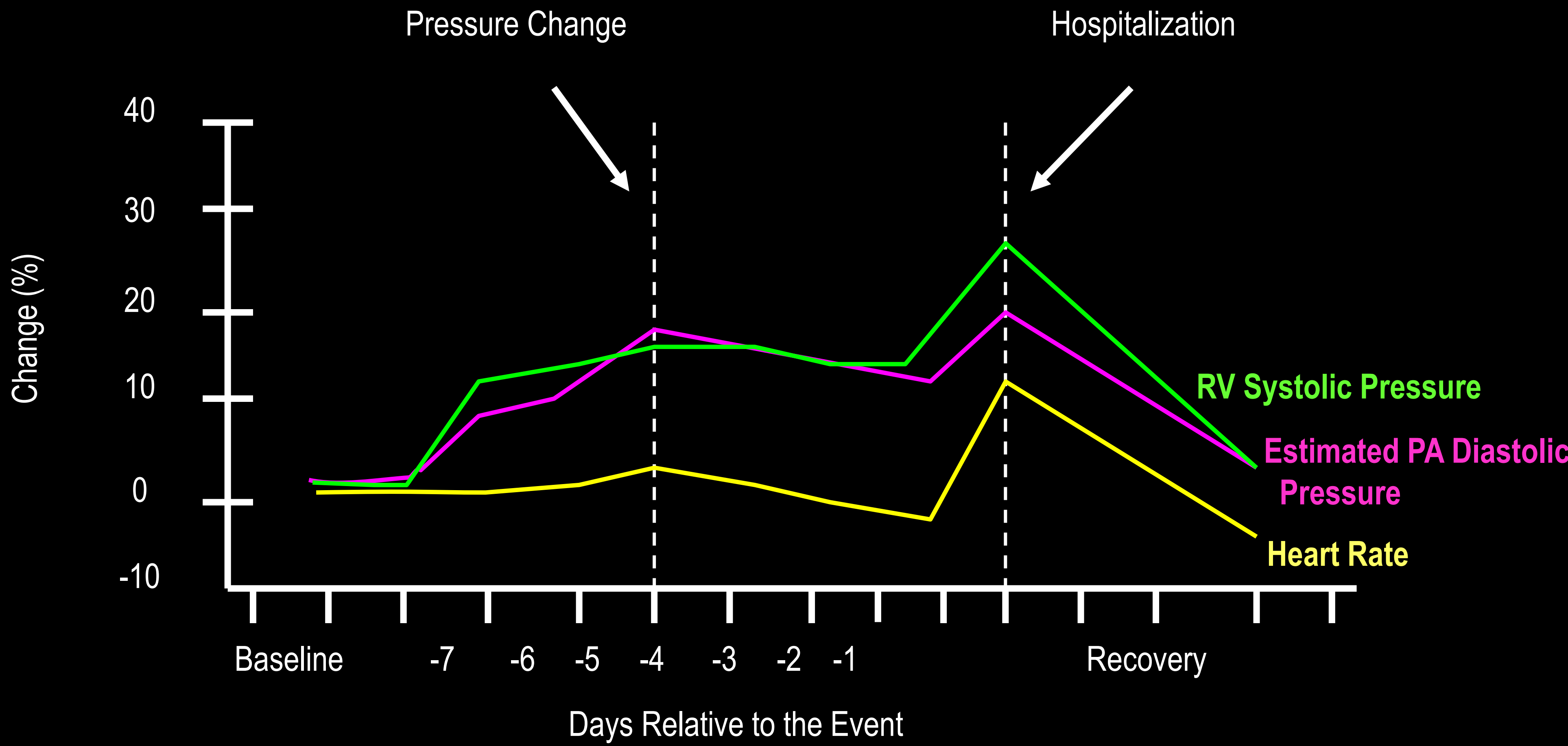
Gheorghiade M et al. Eur J Heart Fail 2010;12:423-433

Sensitivity of weight gain as low as 17 - 20%

Implanted Devices (CRT, ICD) Based Parameters

Lung congestion starts about 2 weeks prior to symptoms

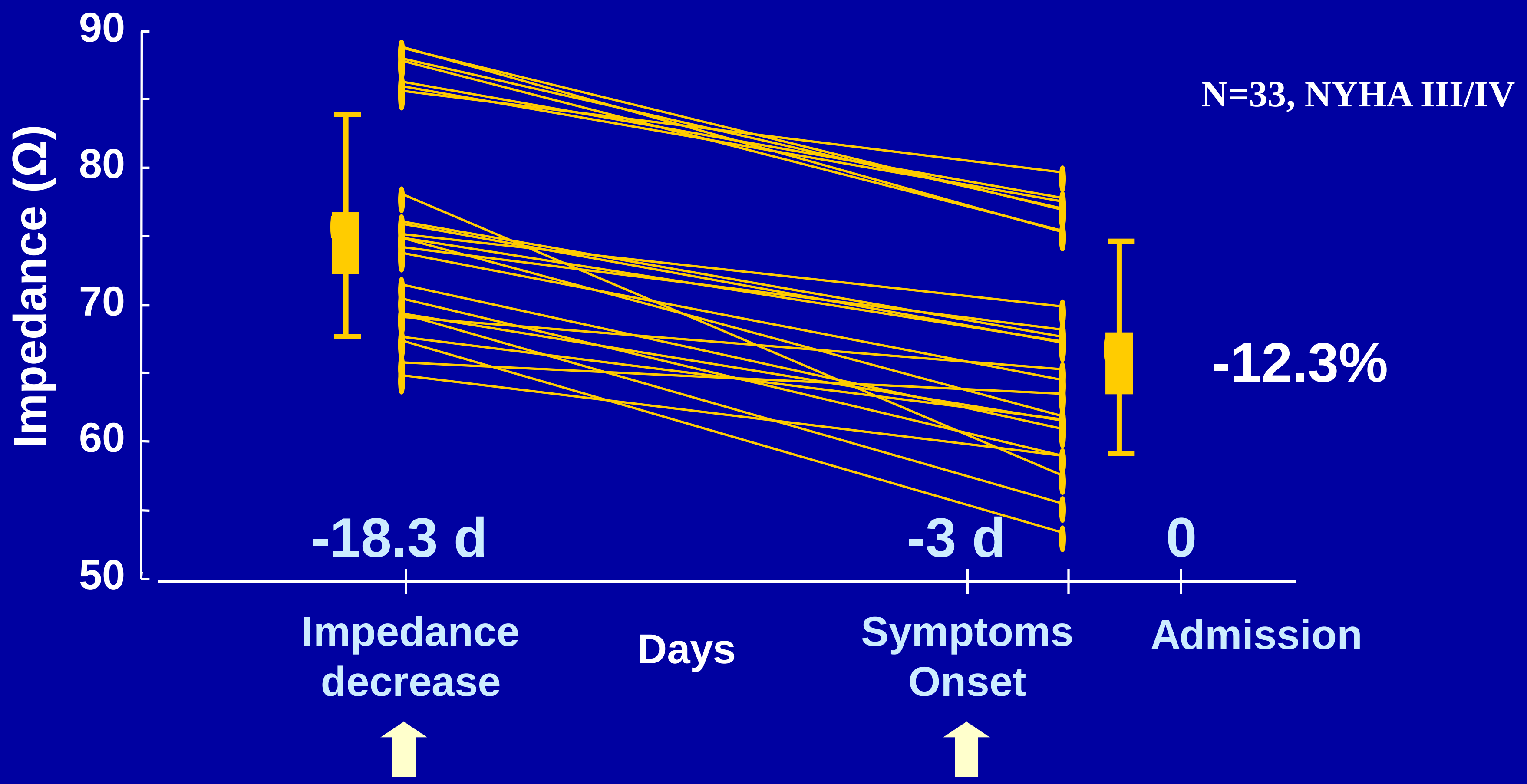
Congestion Precedes Hospitalization



Adamson PB et al. J Am Coll Cardiol. 2003; 41: 565

Intrathoracic impedance: MIDHeFT

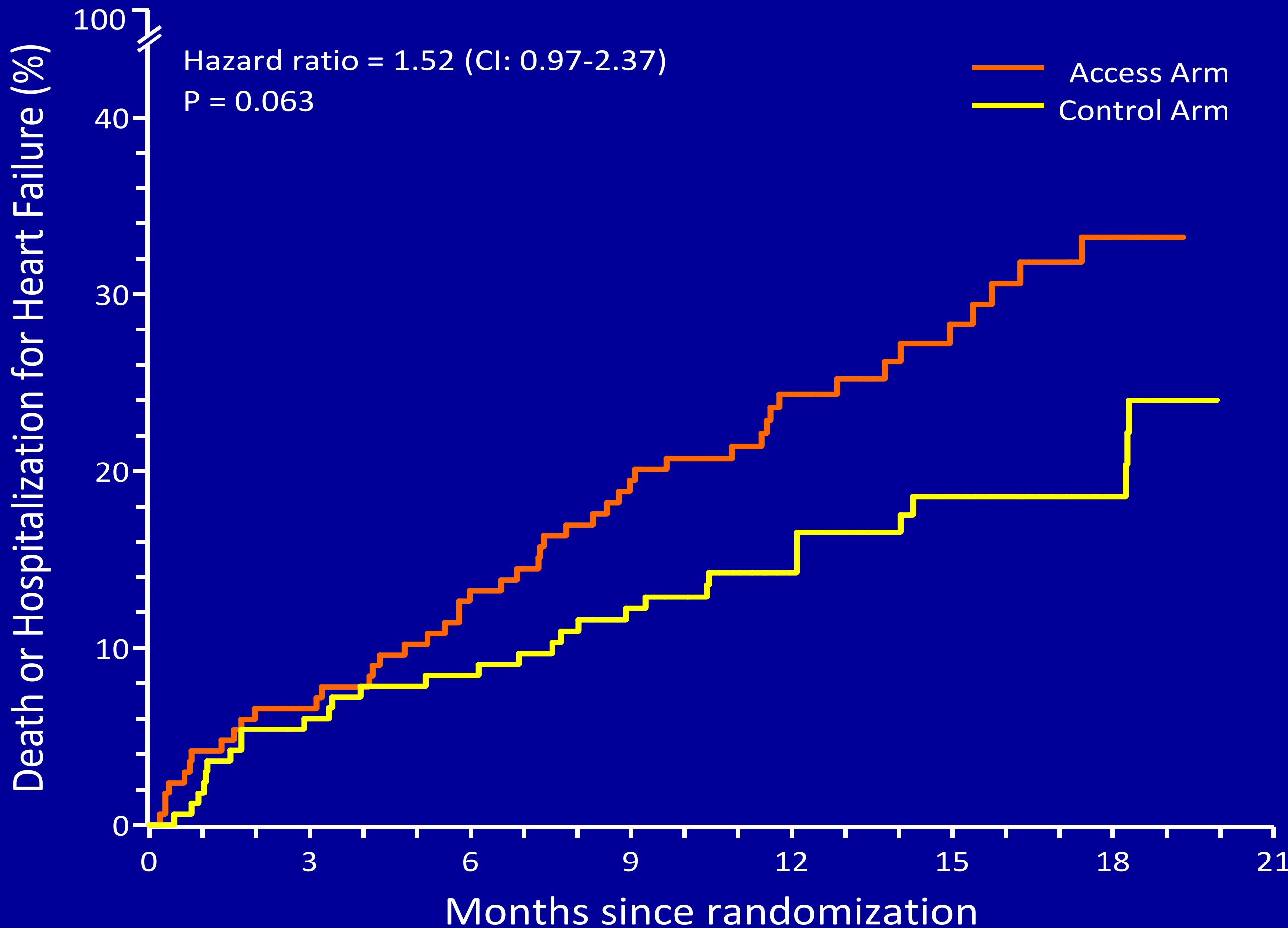
Impedance reduction prior to admissions



Decline in impedance preceded symptoms onset by 15.3 days (p<0.001)

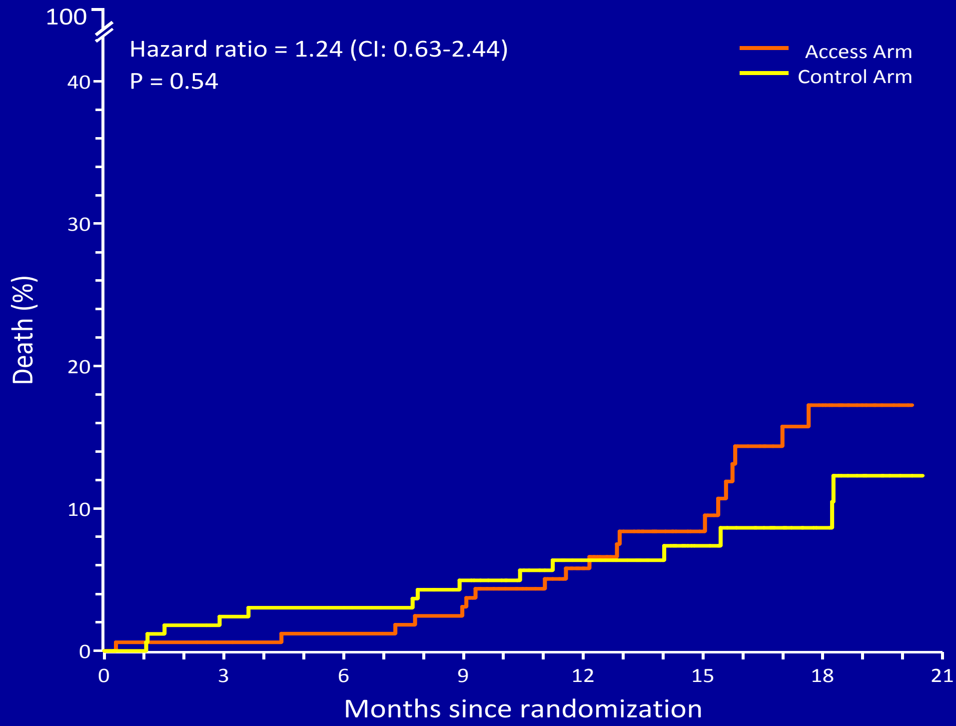
Yu CM et al, Circulation 2005;112:841-848

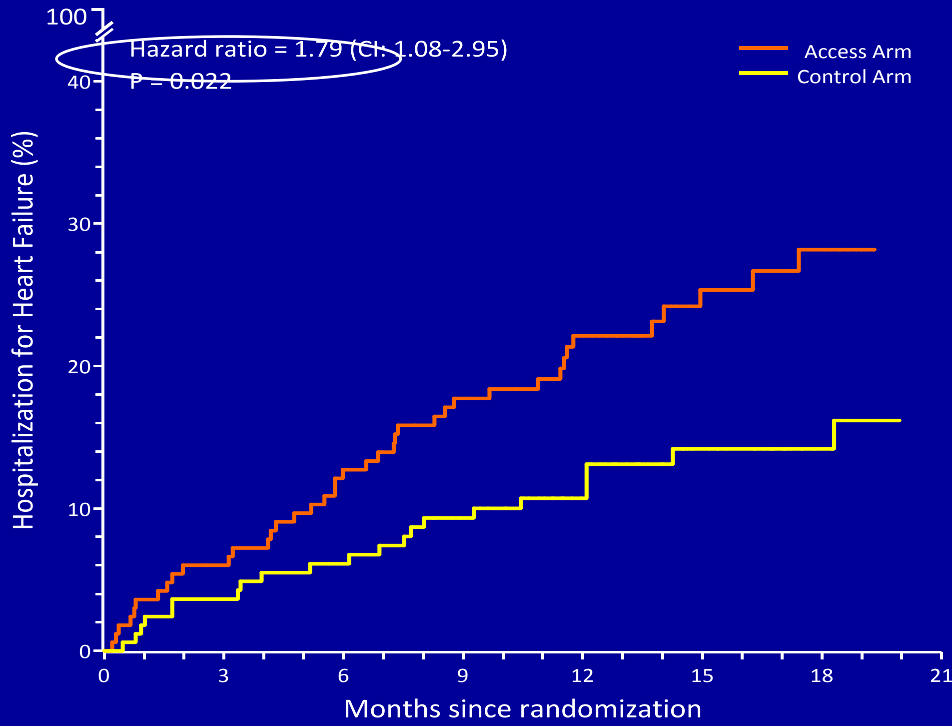
DOT-HF trial primary endpoint
all-cause mortality and HF hospitalization in 335 patients



No. at Risk							
Access Arm	168	156	144	130	97	66	47
Control Arm	167	156	151	136	113	67	46

DOT-HF trial components of primary endpoint





all-cause mortality

19 in Access Arm
15 in Control Arm

HF hospitalizations

60 in Access Arm (41 pts)
36 in Control Arm (24 pts)

Is There Light at the End of the Tunnel? The In-Time Trial

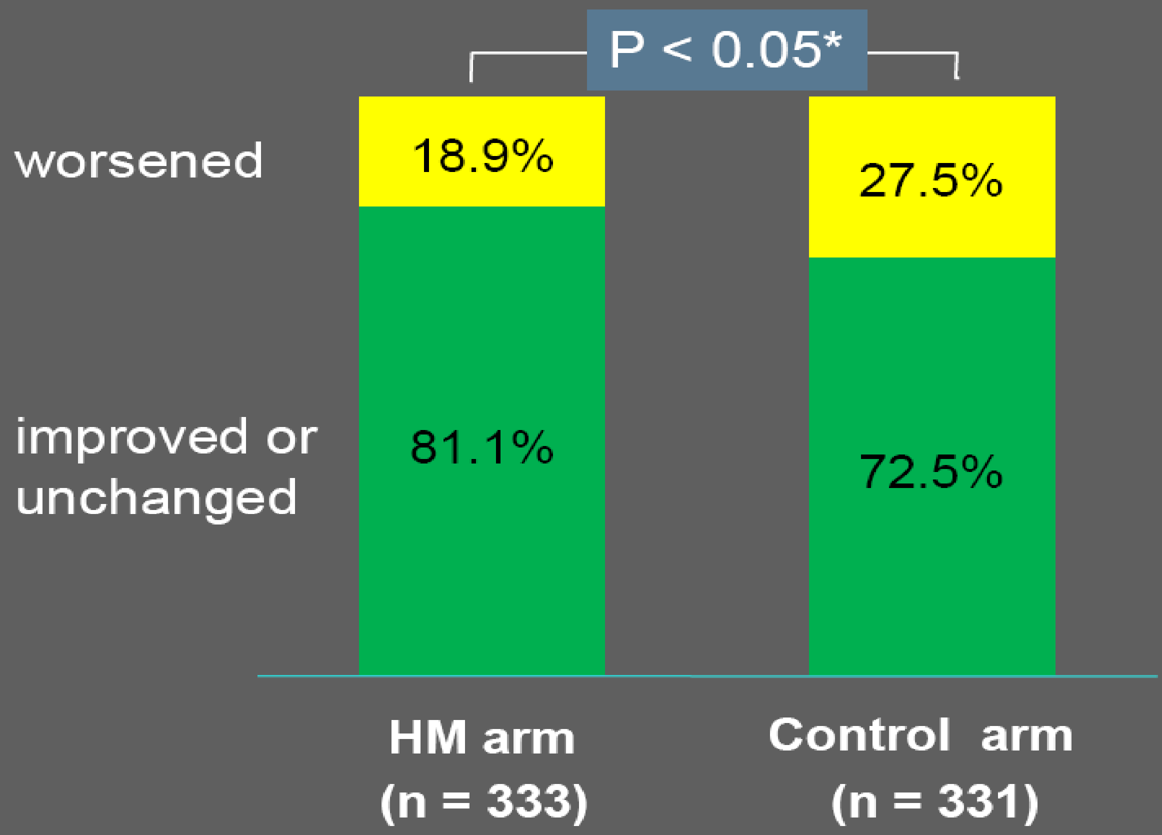
IN-TIME: The Influence of Implant-Based Home Monitoring on the Clinical Management of Heart Failure Patients with an Impaired Left Ventricular Function

- Prospective, randomized, controlled, multicenter trial
- 664 patients, mean age 66±9 years, with chronic heart failure lasting for 3 months or more, class II or III New York Heart Association (NYHA) symptoms
- Reduced left ventricular ejection fraction (LVEF) of ≤35%
- With either CRT/D (59%) or ICD (41%)

Hindricks G et al. ESC Congress, Amsterdam 2013

Home Monitoring and Heart Failure: The In-Time Trial

Results: modified Packer Score



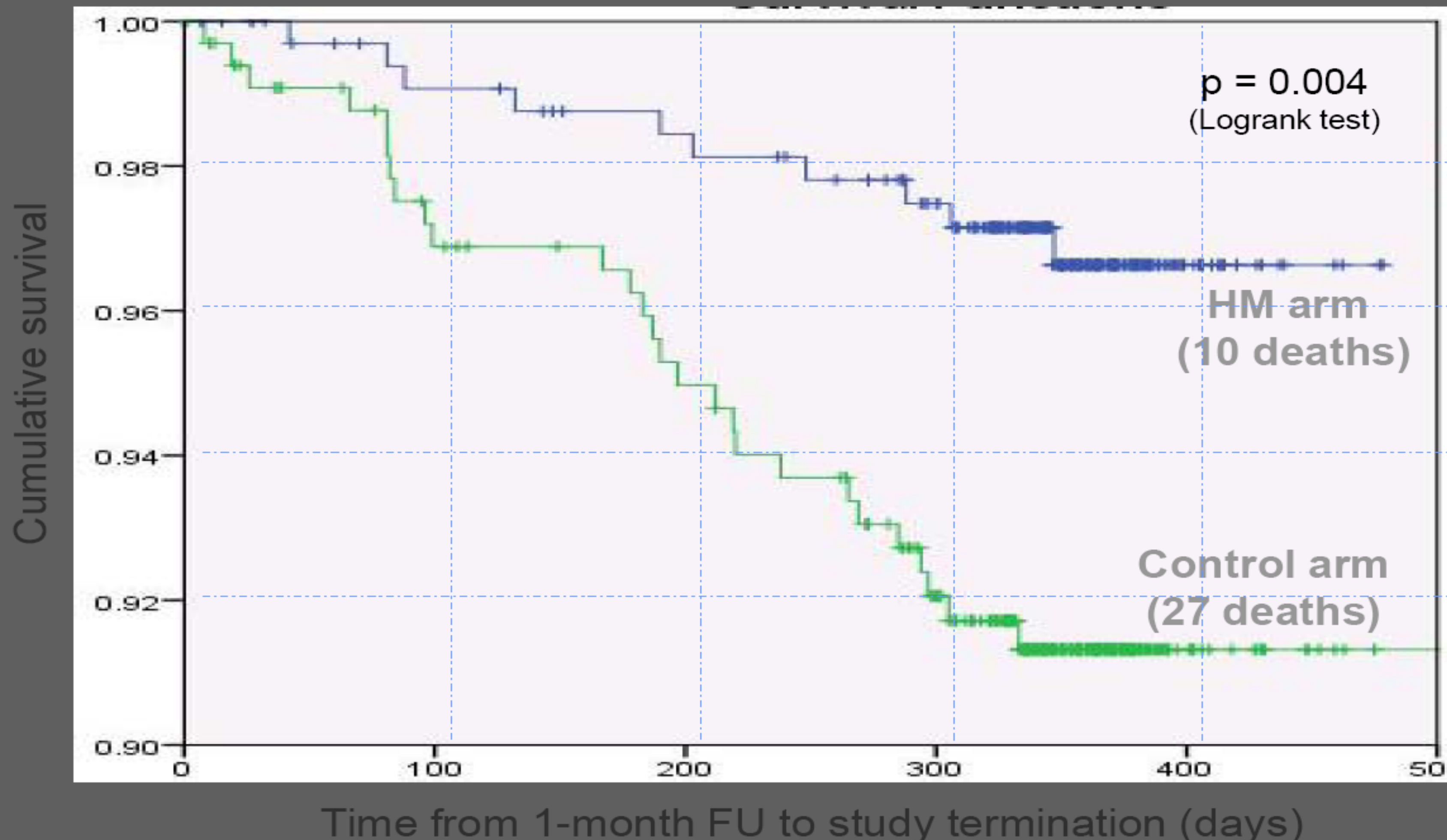
*χ2 test

Hindricks G et al. ESC Congress, Amsterdam 2013

Home Monitoring and Heart Failure: The In-Time Trial

All-cause mortality

HR: 0.356 (95% CI: 0.172–0.735)

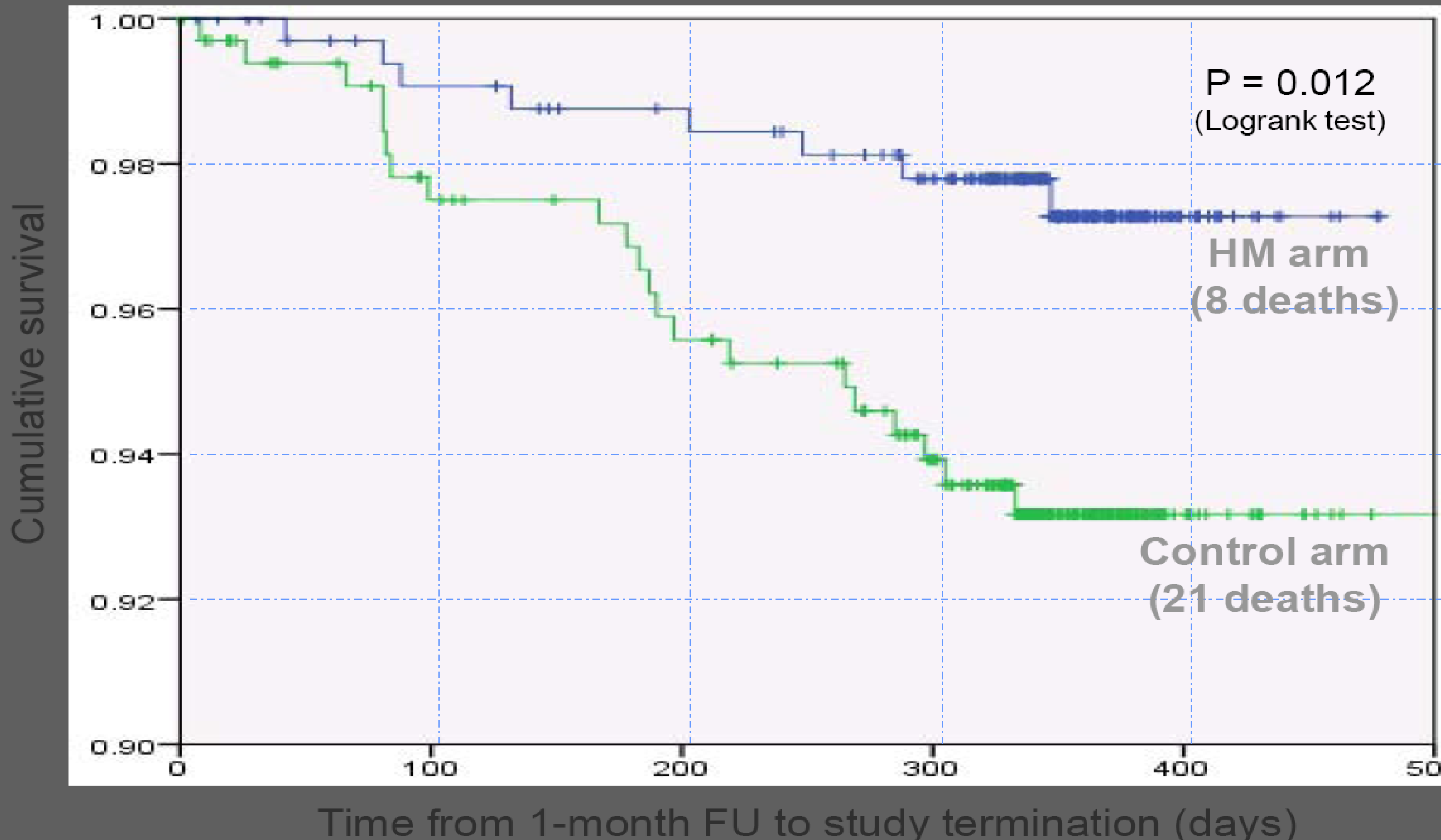


Hindricks G et al. ESC Congress, Amsterdam 2013

Home Monitoring and Heart Failure: The In-Time Trial

Cardiovascular mortality

HR: 0.367 (95% CI: 0.162–0.828)



Hindricks G et al. ESC Congress, Amsterdam 2013

Home Monitoring and Heart Failure: The In-Time Trial

Conclusions

- In-Time is the first implant-based remote monitoring RCT demonstrating significant benefits of implant-based home monitoring for patients with advanced heart failure.

- In the home monitoring arm of the trial:
  - the number of heart failure patients with worsening of the clinical status was significantly reduced.
  - total mortality and cardiovascular mortality were significantly reduced compared to standard care.

- Home monitoring based detection of changes in clinical status or technical events can trigger medical action that prevents worsening of heart failure.

Hindricks G et al. ESC Congress, Amsterdam 2013

Implanted Sensors/Hemodynamic Monitors

Sensor Modalities for Heart Failure Monitoring

Merchant FM, Singh JP. Circulation 2010;3:657-667

Sensor	Examples
Currently available sensors	
Heart rate derivatives	Mean heart rate, nocturnal heart rate
	Heart rate variability (SDAAM, SDANN)
	HRV footprint
Accelerometers	Physical activity level
Impedance monitors	RV-Can (OptiVol)
	LV-RV, LV-can impedance
	Minute ventilation
Hemodynamic	Right ventricle pressure (Chronicle IHM)
	RV dP/dt_{max} (ePAD)
	Left atrial pressure (HeartPOD)
	Pulmonary artery pressure (Champion)
Cardiac output	Doppler
	RV O_2 saturation monitor
Heart sounds	Peak endocardial acceleration
Emerging modalities	
Chemicals	Po_2, Pco_2, pH
	Electrolytes, glucose
Biomarkers	Natriuretic peptides (BNP, NT-proBNP, ANP)
	Inflammatory markers (TNF-a, IL-6, hsCRP)
	Troponin
Metabolomic/signaling cascades	Apoptosis/caspase signaling
	Glycolysis
	Microtubule assembly pathways

champion

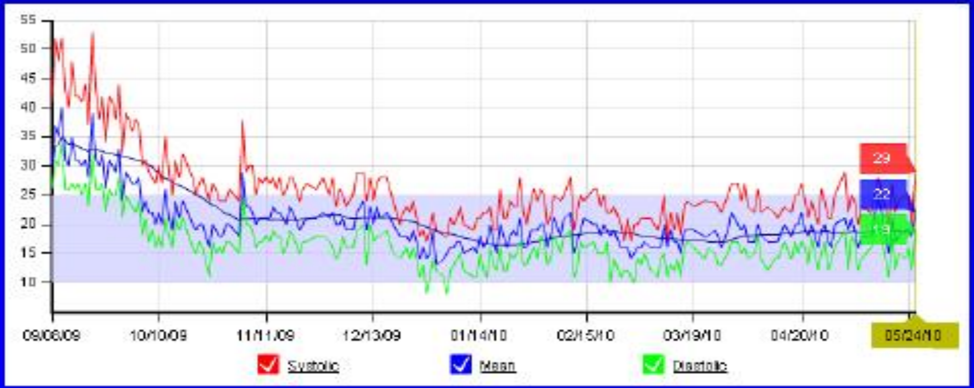
The Pulmonary Artery Pressure Measurement System*

Catheter-based delivery system

MEMS-based pressure sensor

Home electronics

PA Measurement database



*CardioMEMS Inc., Atlanta, Georgia, USA

Caution – Investigational device. Limited by United States law to investigational use

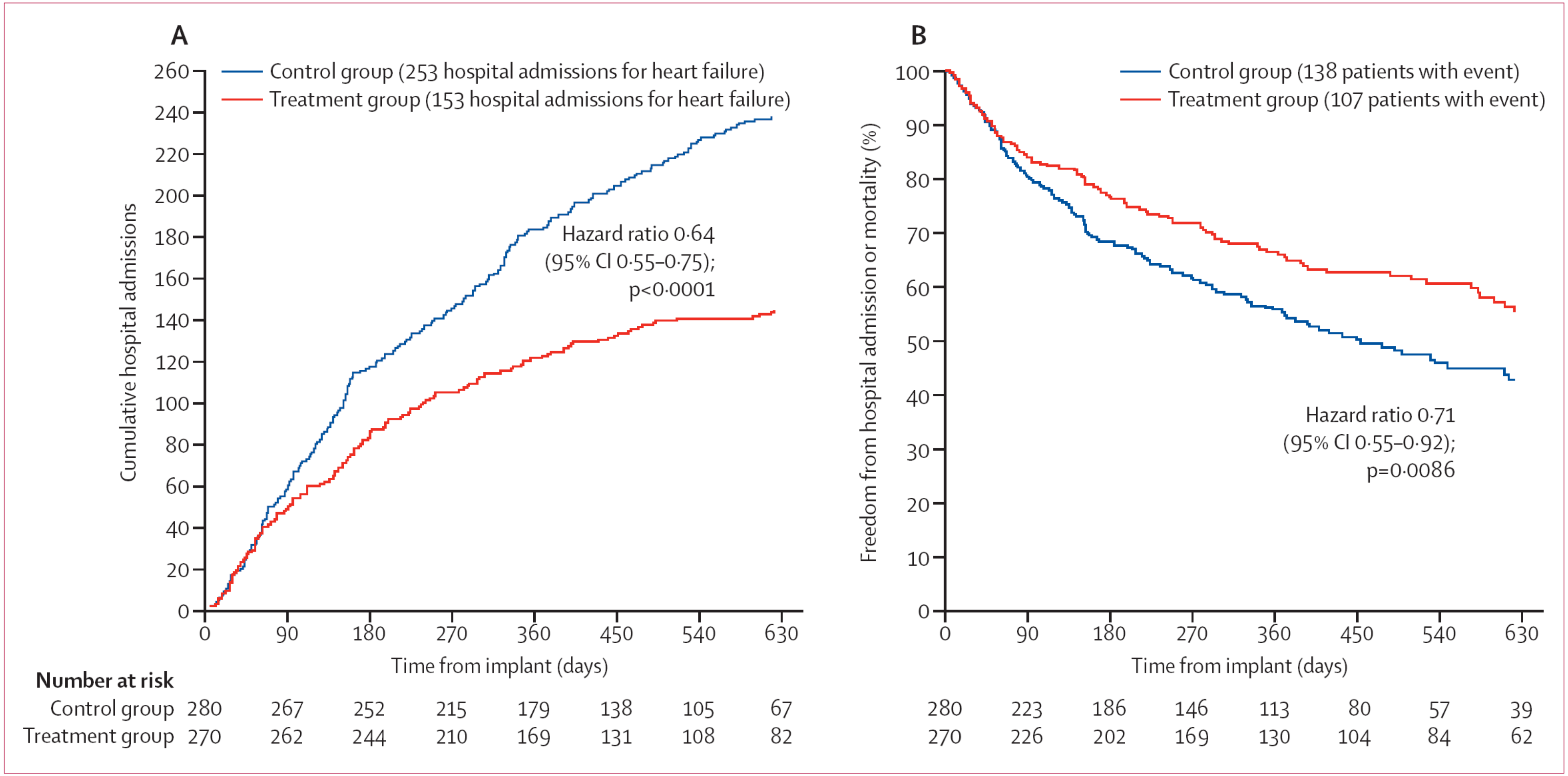


***Figure 3:* Cumulative heart-failure-related hospitalisations during entire period of randomised single-blind follow-up (A), and freedom from first heart-failure-related hospitalisation or mortality during the entire period of randomised follow-up (B)**

Abraham WT, Lancet 2011;377:658-666

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®
Learn and Live℠

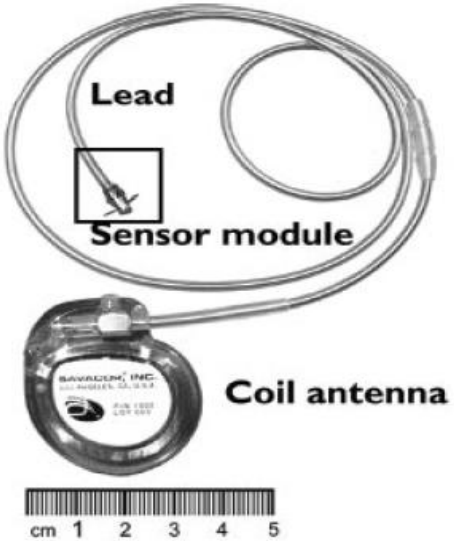
Physician-Directed Patient Self-Management of Left Atrial Pressure in Advanced Chronic Heart Failure

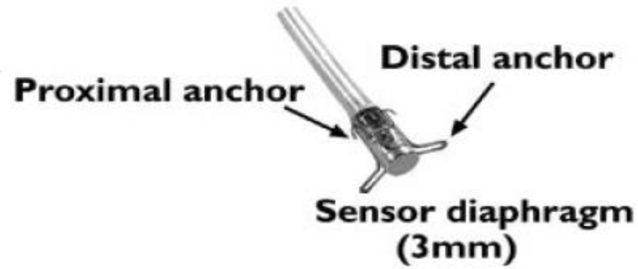
Jay Ritzema, Richard Troughton, Iain Melton, Ian Crozier, Robert Doughty, Henry Krum, Anthony Walton, Philip Adamson, Saibal Kar, Prediman K. Shah, Mark Richards, Neal L. Eigler, James S. Whiting, Garrie J. Haas, J. Thomas Heywood, Christopher M. Frampton and William T. Abraham

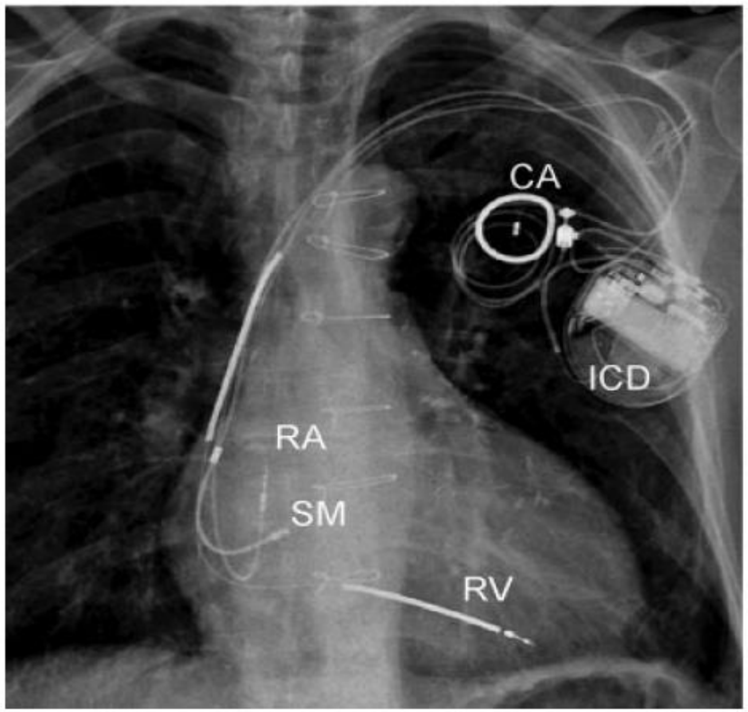
Circulation 2010, 121:1086-1095: originally published online February 22, 2010

HeartPOD, St Jude Medical Inc, Minneapolis, Minn, USA

Homeostasis I&II







PAM **(Patient Advisory Module)**

Ritzema J et al. Circulation 2010;121:1086-1095

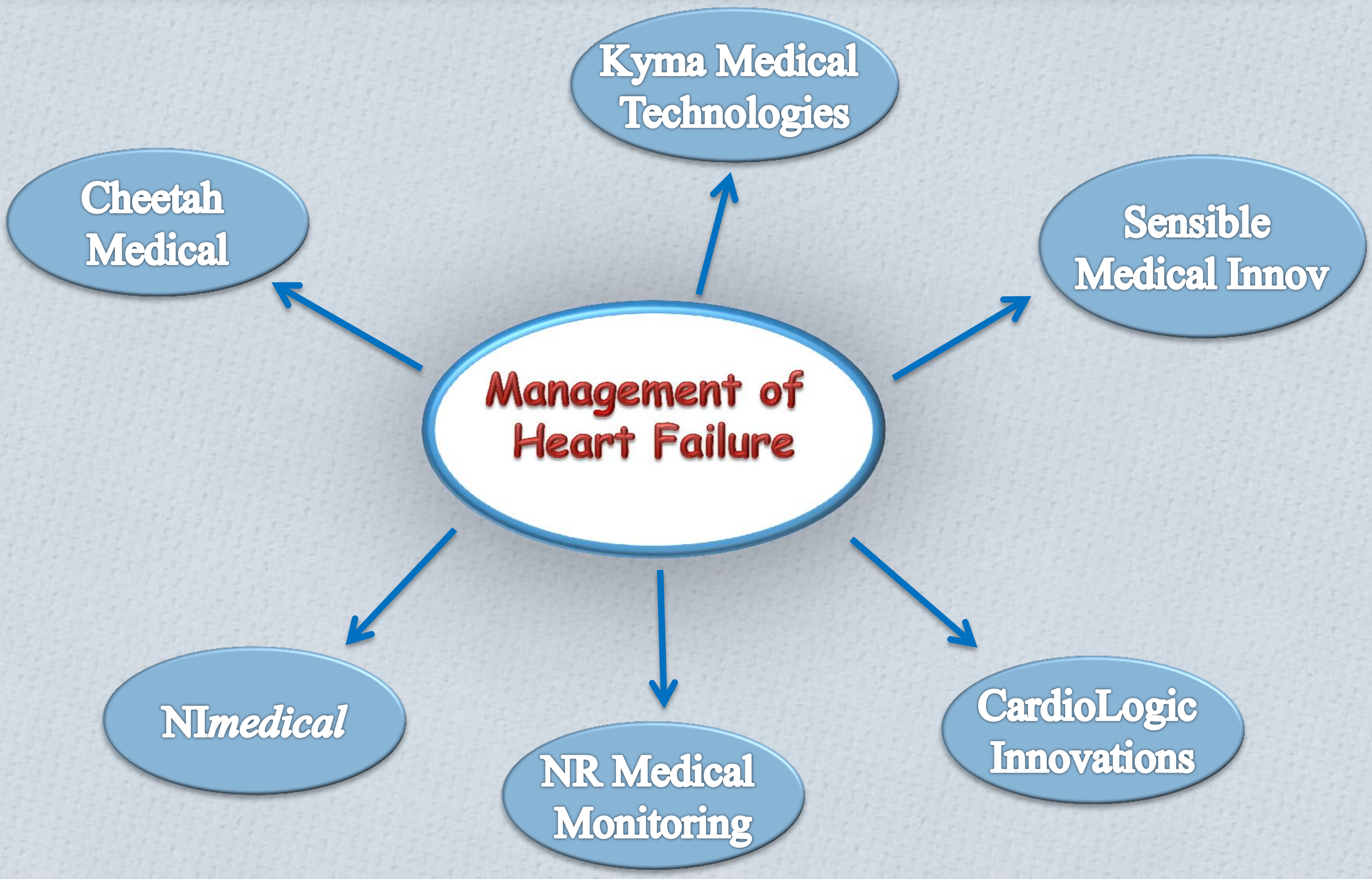
RESULTS

- Device was safe
- Medications
  - ACE inhibitors/ARBs uptitrated by 37% ($p<0.001$)
  - beta blockers uptitrated by 40% ($p<0.001$)
  - diuretics downtitrated by 27% ($p=0.15$)
- NYHA class improved by 0.7 class ($p<0.001$)
- LVEF% increased by 7% ($p<0.001$)
- Lower risk of admission due to ADHF ($p=0.012$)[32-96%]

Ritzema J et al. Circulation 2010;121:1086-1095

Quo Vadis?

Israel, the Promised Land of HF Devices



Cheetah Medical
Fluid Optimization Machines™

NICOM® Technology

HOW DOES IT WORK?

ss Releases | f | YouTube
urve Tutorial | FAQ

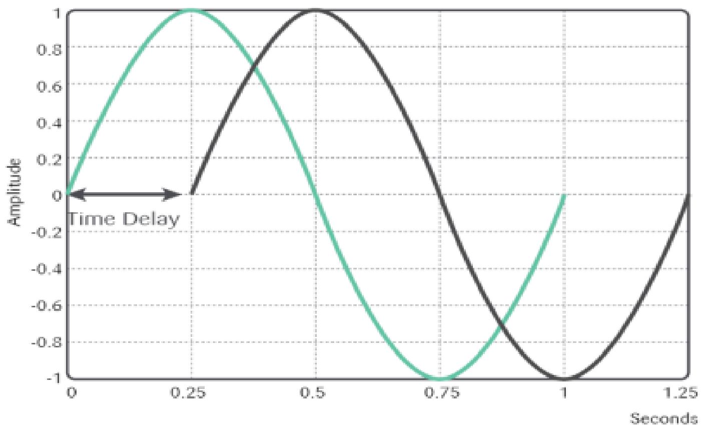
Introduction

NICOM enables continuous, accurate, non-invasive hemodynamic monitoring in any clinical setting. It is based on Bioreactance, or the Phase Shifts that occur when an alternating current is passed through the thorax. NICOM should not be confused with the measurement of bio-impedance, an older and less accurate technology.

To comprehend this unique and proprietary technology one must first get acquainted with the term 'Phase Shift'.

What is a Phase Shift?

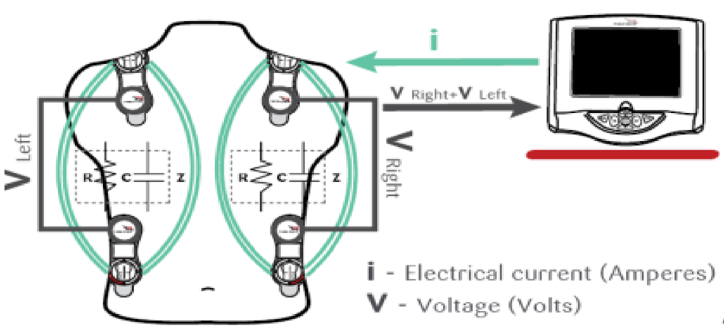
Figure 1 - Phase Shift As Time Delay



When an alternating current (AC) is applied to the thorax, the thoracic pulsatile blood flow through the large arteries causes the amplitude of the applied thoracic voltage to change. In addition, it causes a time delay or Phase Shift between the applied current and the measured voltage.

Extensive research has shown that these Phase Shifts are tightly correlated with stroke volume. By accurately and continuously measuring Phase Shifts one is able to determine the stroke volume. NICOM is equipped with a sensitive phase detector that can detect very small Phase Shifts.

Figure 2 - Electrical Equivalence of the Thorax



Kyma's µCor®
Continuous Remote Monitoring of Thoracic Fluid

Direct and accurate measurement of thoracic fluid & vital signs

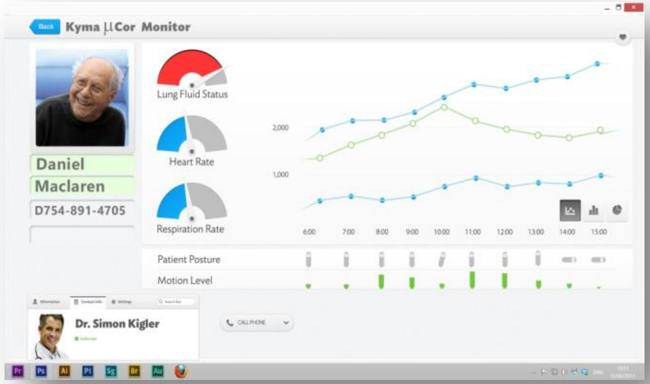
Based on a body-penetrating radar (electromagnetic) technology

Provides early warning (5-7 days) of pulmonary congestion

Trials

- Accuracy proven using Thermodilution as a reference
- Extensive clinical & preclinical trials in homes and in hospitals – RICU, Internal Ward, Day-Care, in Kaplan, Sheba & US healthcare facilities

CE marked, FDA in process

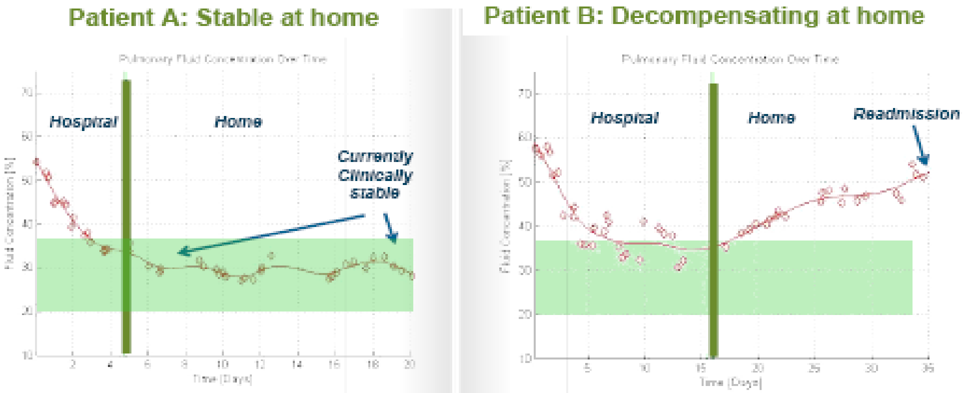


Remote Dielectric Sensing (ReDS) Technology

Non-Invasive Assessment of Lung Water

- Proprietary RF monitoring and imaging technology*
- As fluid replaces air, there is an increase in the dielectric coefficient
- Measurement is localized (lung-specific) as opposed to other modalities (e.g., bio-impedance)
- Enables non-invasive and continuous monitoring of lung fluid concentration

ReDS Observational Study: Hospital-to-Home



Under current protocol physicians are blinded

Amir O, Abraham WT et al. Congest Heart Fail 2013;19:149-155

Abraham WT, ESC Congress Amsterdam 2013

NImedical

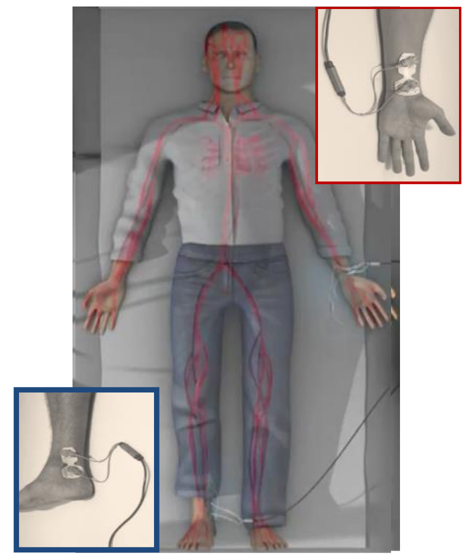
Whole Body Impedance Cardiography

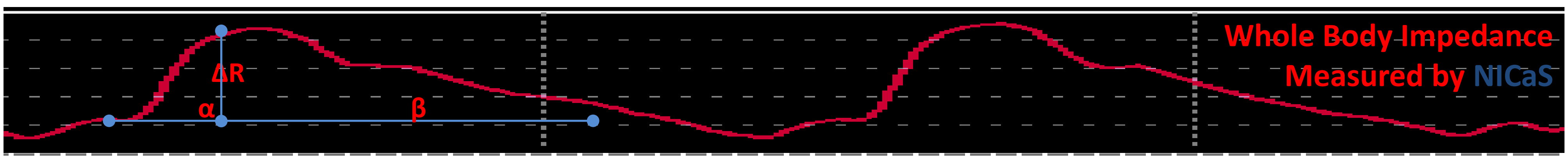
NICaS (Non Invasive Cardiac System) ability to accurately trend major vital signs inc. **Stroke Volume**, **Cardiac Output**, **Total Peripheral Resistance** and **Total Body Water**, in the community, enable to better manage **CHF** patients and keep them **out of the hospital**

♥ **NICaS** measures changes of elect' resistance in the arterial system, through two sensors arranged in a wrist-to-ankle configuration, and convert them to changes in quantities of blood

♥ **Stroke Volume**, **Cardiac Output**, **Total Peripheral Resistance** and **Total Body Water** are calculated by proprietary algorithms

♥ The **Whole Body Impedance** technology is unique and superior to any other, Thoracic based, Cardiac Output measuring technologies and the **only technology that is within the boundaries of the FDA guidelines of bio-equivalence***

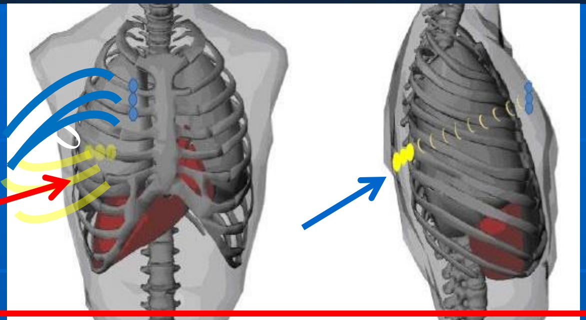




* O. Paredes et al: Impedance Cardiography for Cardiac Output Estimation, Circulation J. 2006; 70:1164-1168

RS MEDICAL MONITORING

New opportunities in Heart Failure Care



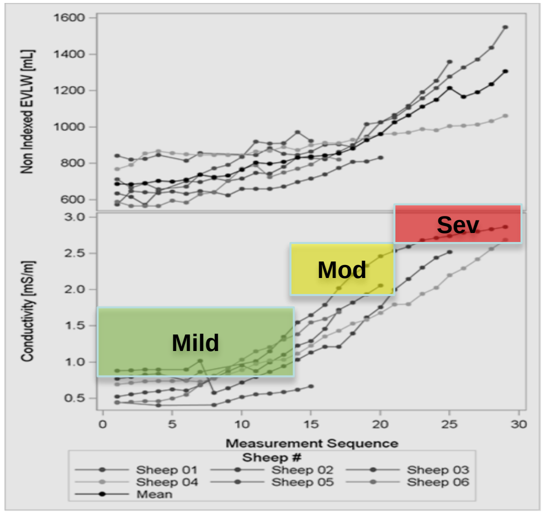
Direction of signal through the chest

Employment of the device:

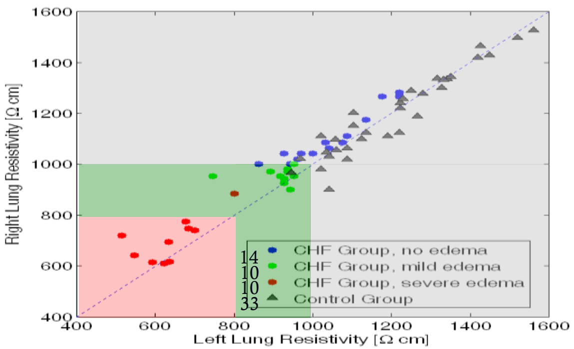
1.Reduced AHF episodes after AMI.
2.Reduced in-hospital and 6-years mortality after AMI.
3.Reduced by 50% re-hospitalizations for AHF and by 40% HF Death in out of hospital setting in CHF patients.

1.	650	Healthy Volunteers	Detection of Lung Impedance (LI) was done to build a model of normal baseline Lung Impedance. *M. Shochat. Eur J Heart Fail 2013;15: P 674*
2.	700	Prediction and prevention AHF in course AMI.	Preemptive treatment based on LI monitoring reduce in hospital and 6 years mortality. Correlation between serial chest X-rays and LI was r= - 0.9. *M. Shochat. Cardiovasc Revasc Med. 2006;7:41-5. Intensive Care Med. 2006;32: 1214-21. Acute Card Care. 2011;13:81-8. Am J Cardiol. 2012;110:190-6*.
3.	230	CHF in outpatient clinic.	LI-guided preemptive treatment of CHF patients reduce re-hospitalization rate and mortality during mean 32 months treatment. *M. Shochat. Eur Heart J. 2013;34:* Evaluation of effectiveness in-hospital anti-congestion treatment by LI.. *Eur Heart J. 2013;34: P1506.*
4.	120	CHF in outpatient clinic.	Comparison of effectiveness BNP and LI monitoring for prediction AHF hospitalizations in CHF patients. *M. Shochat. Eur J Heart Fail 2013;15:P 939.*
5.	45	Severe CRF on hemodialysis.	Monitoring was done for proving the hypothesis that removal of fluid by dialysis Increase a Lung Impedance. *Unpublished data.*

Parametric Electrical Impedance Tomography (*pEIT*™)



Keren A. ICI 2013 Abstract



Zlochiver et al. Congest Heart Fail. 2005

- CardioLogic Innovations Ltd. EIT is based on a proprietary algorithm and technology of electrical signals processing and spatial reconstruction
- Determines fluid levels in each lung in isolation from other organs in the thorax (Conductivity)
- Good correlation with pulmonary congestion in an animal model compared with EV1000 (Edward Lifescience)
- Good correlation with clinically defined pulmonary congestion in pilot clinical studies

Hospital & out patient clinic

Add on module for implantable devices

Home Monitor

HF-monitoring: Unmet Needs

- Remote monitoring is a very promising technology
- At that point in time we still do not know:
  - Which are the best parameters to be monitored
  - What are the best algorithms to avoid TMI (too much information) and alter promptly therapies, if indicated
  - Who should be the receiver of the information & in charge of changes in Rx
  - What is the appropriate Nurse : Patient ratio (NNNT-P)

Thank you