Heart failure and CRT : new topics and evidence in 2015

The integrated approach of multiple parameters to monitor the HF worsening

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UOSD di Elettrofisiologia, Studio e Terapia delle Aritmie

AORN "Dei Colli – Osp. V. Monaldi"

NO CONFLICT OF INTEREST

TO DECLARE

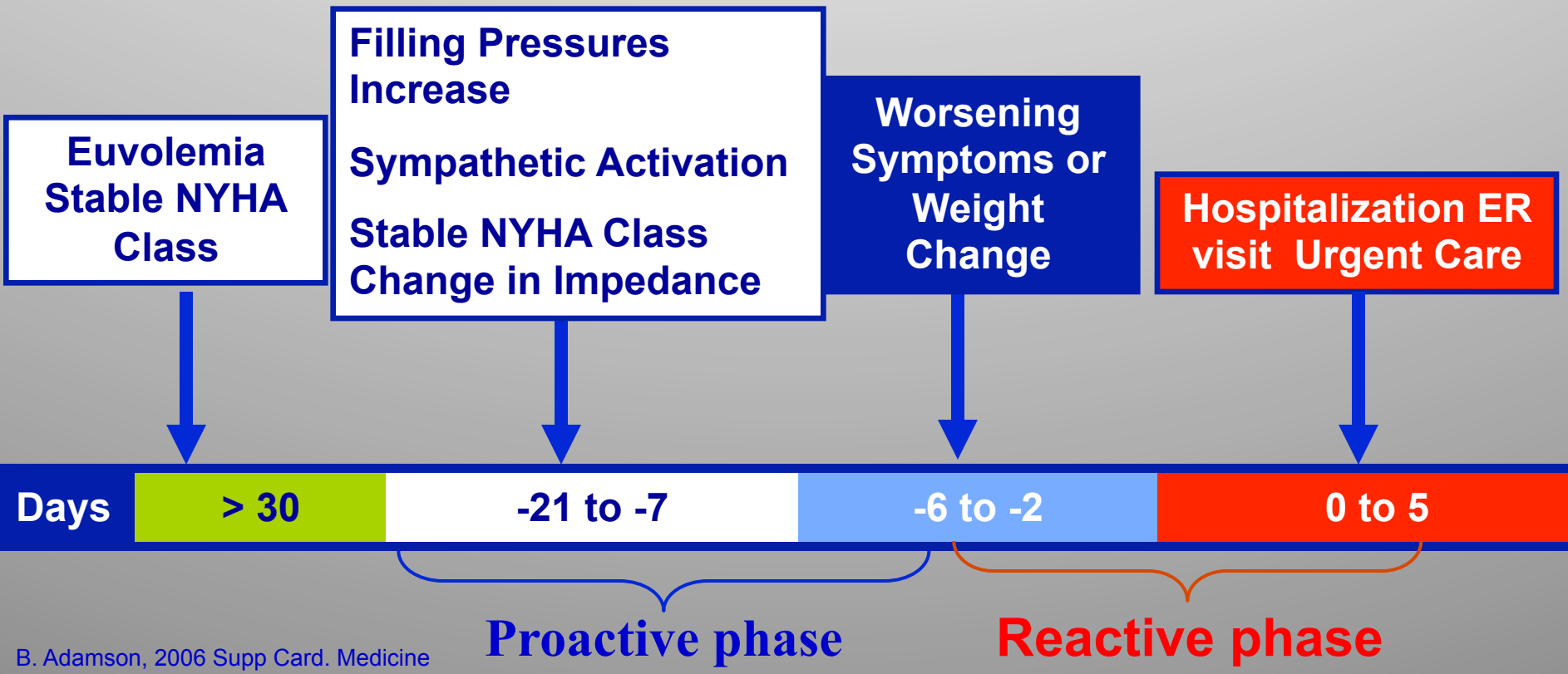
- **Heart failure remains one of the largest medical problems of our time.**
- **It is a very costly disease, and in 2010, its total cost in the United States alone was estimated to be $39.2 billion.**
- **Close monitoring is crucial and can be done through a whole spectrum of modalities and systems.**
- **This monitoring ranges from a nurse-based disease management program, to structured telephone support, to remote or telemonitoring with or without the use ICD or ICD CRT**

Early detection of worsening heart failure by a monitoring implant could enable pre-emptive medical intervention and improve outcomes beyond those achieved with stand-alone implantable devices.

Early diagnosis and intervention may play a crucial role in minimizing major cardiovascular events and reducing hospitalizazion

Acute HF event prevention

Pulmonary congestion is difficult to recognize in its early stages of development because of the late appearance of symptoms before hospitalization



B. Adamson, 2006 Supp Card. Medicine

Classification of HF Monitoring Systems

HF Monitoring Systems

- **Invasive Systems**
- **Non-Invasive Systems**

- **Baseline/Cross-sectional predictors**
- **Longitudinal Predictors**

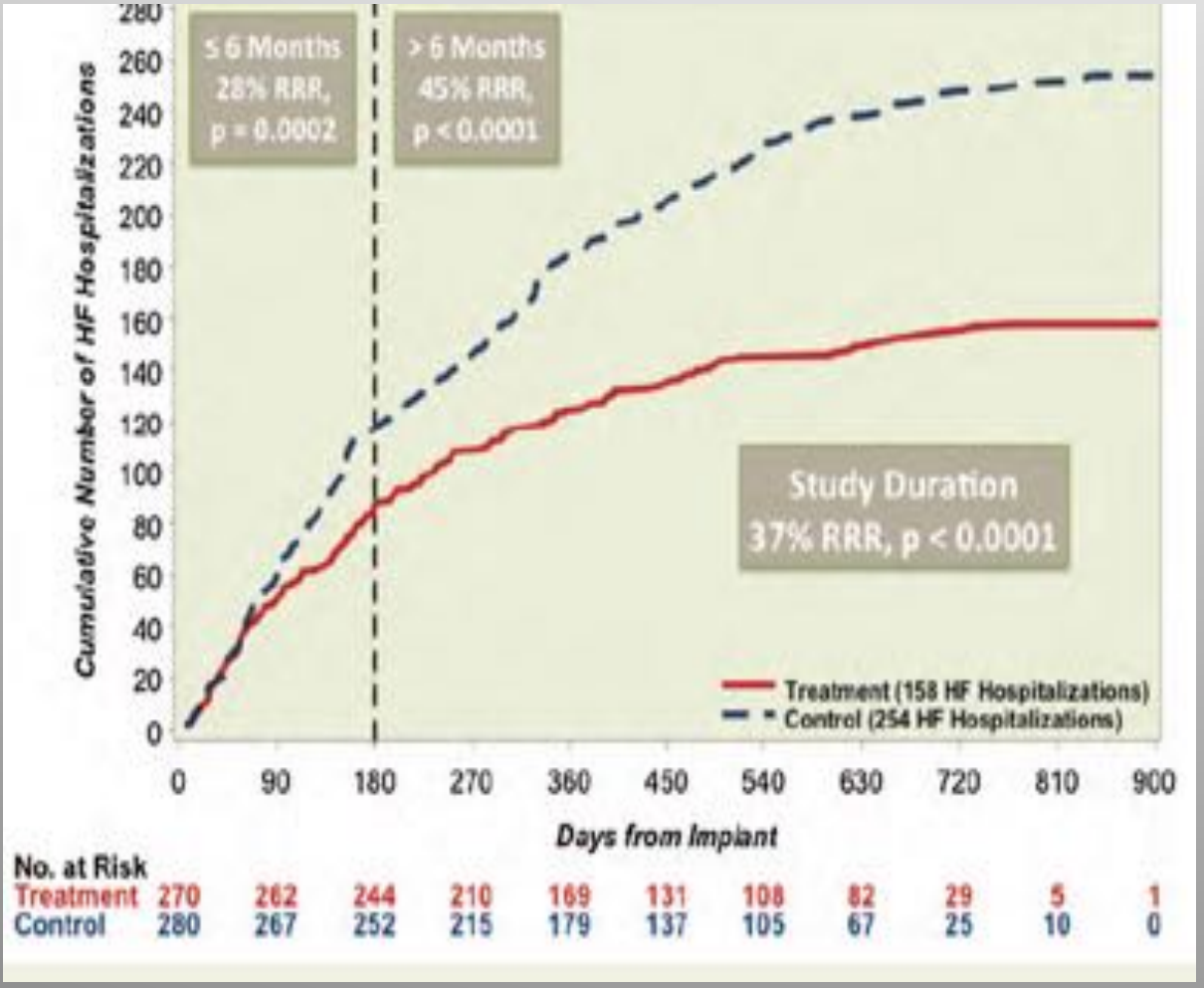
Invasive monitoring system

Invasive variables

Pulmonary artery pressure	Daily	Automatic(with PTS operated interrogation)
Left atrial pressure	Daily	Automatic
Impedence	Daily	Fully automatic
Detection of life-threatening Arrhythmias in addition to Atrial fibrillation or Ventricular Tachicardia	Daily	Automatic

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, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group*



The use of pulmonary artery pressure measurement system has been shown to significan tly reduce risk of heart failure hospitalization in a large randomized controlled study

Lancet, 2011; 377: 658-666 - CHAMPION Trial

Invasive Monitoring

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, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group*

Prospective, multicentre, single-blind, clinical trial undertaken in 64 centers in the USA. 550 Pts with NYHA class III heart failure.

***Lancet*, 2011; 377: 658-666_CHAMPION Trial**

Invasive Monitoring

Rationale and Design of the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy Study (LAPTOP-HF)

MATHEW S. MAURER, MD,[1] PHILIP B. ADAMSON, MD,[2,3] MARIA ROSA COSTANZO, MD,[4] NEAL EIGLER, MD,[5] JOANNE GILBERT,[3] MICHAEL R. GOLD, MD,[6] MARC KLAPHOLZ, MD,[7] LESLIE A. SAXON, MD,[8] JAGMEET P. SINGH, MD, PhD,[9] RICHARD TROUGHTON, MB, ChB, PhD,[10] AND WILLIAM T. ABRAHAM, MD[11]

LAPTOP-HF is a prospective, multicenter, randomized, controlled clinical trial.
It began enrollment in June 2010, and the completion of recruitment and follow-up has been anticipated in 2015

730 Pts with NYHA class III. Includes a HeartPOD implantable sensor lead (ISL) that measures the LAP waveform, core temperature, and the intracardiac electrogram (IEGM)

Journal of Cardiac Failure
Vol. 21 No. 6 2015

Rationale and Design of the Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy Study (LAPTOP-HF)

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The primary safety end point is freedom from study related major adverse cardiovascular and neurologic events

The primary effectiveness end point is the reduction in the relative risk of HF hospitalization

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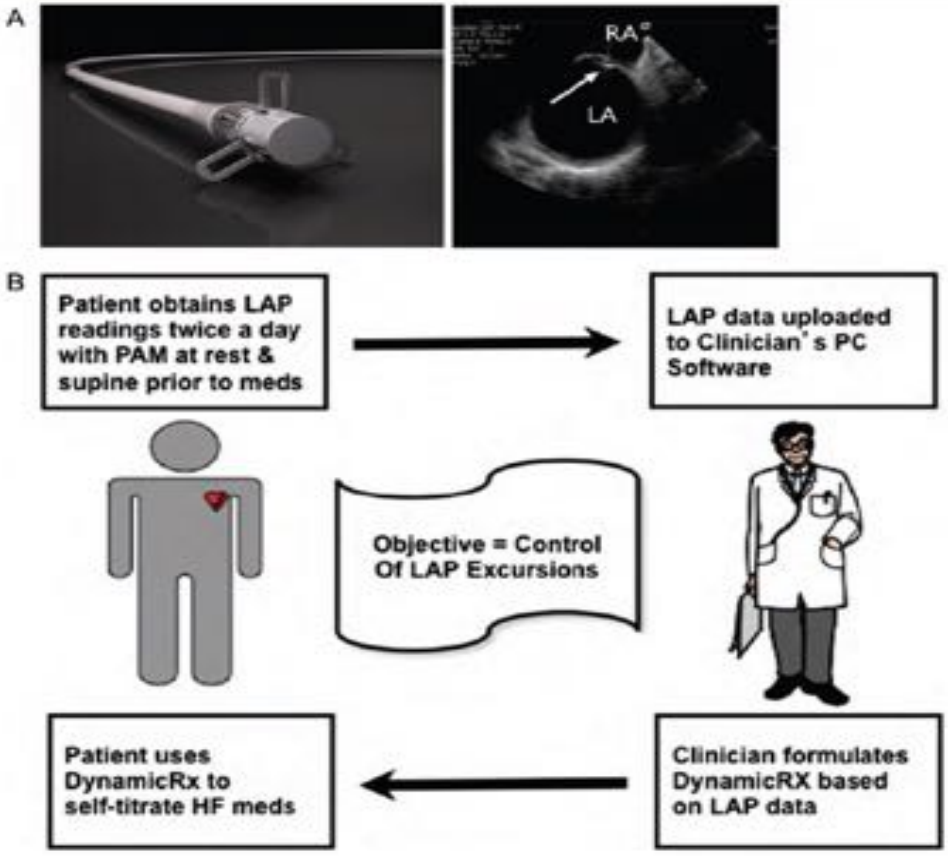

Left Atrial Pressure monitors

LAPTOP-HF is supposed to provide essential information about the role of implantable LAP monitoring.

Journal of Cardiac Failure
Vol. 21 No. 6 2015

Invasive monitoring system

Invasive variables

Pulmonary artery pressure	Daily	Automatic(with PTS operated interrogation)
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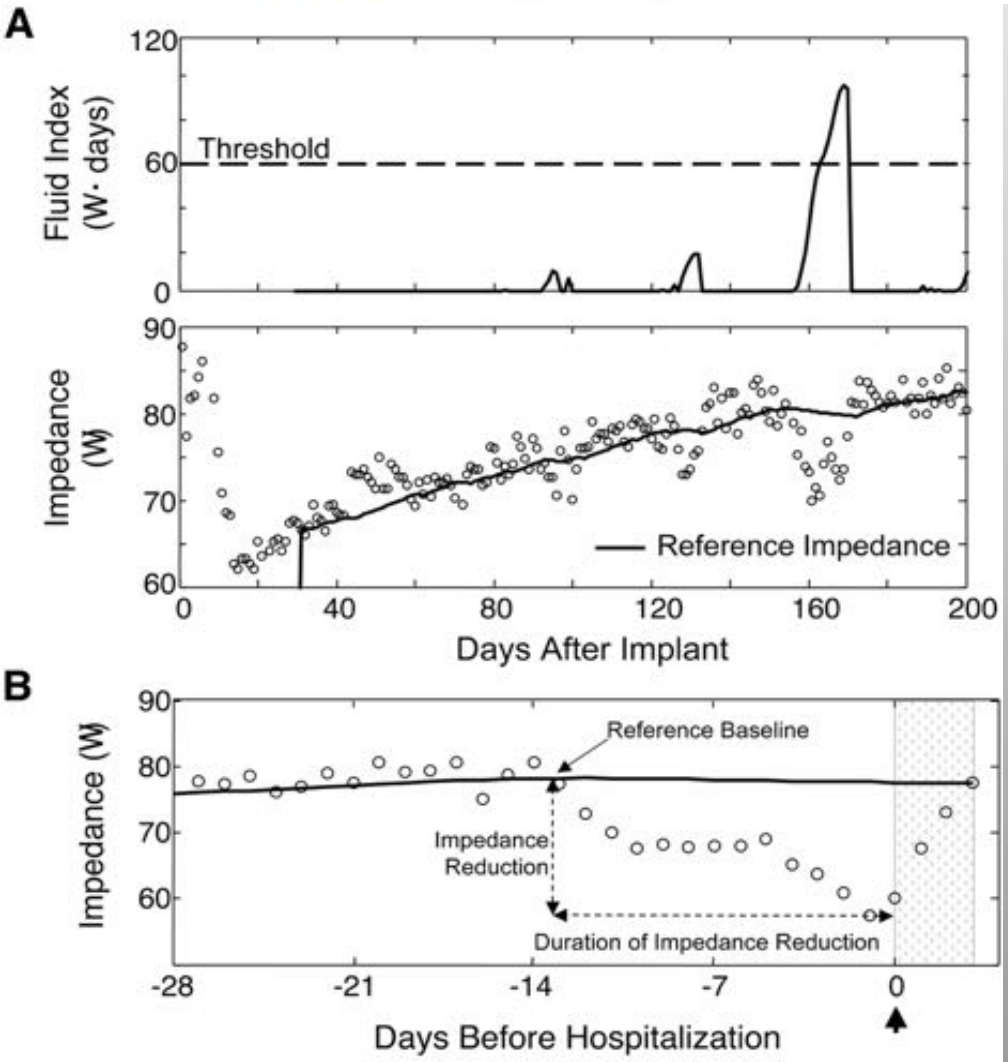
Detection of life-threatening Arrhythmias in addition to Atrial fibrillation or Ventricular Tachicardia	Daily	Automatic

Intrathoracic Impedance Monitoring in Patients With Heart Failure

Correlation With Fluid Status and Feasibility of Early Warning Preceding Hospitalization

Cheuk-Man Yu, MD, FRCP; Li Wang, PhD; Elaine Chau, FRCP; Raymond Hon-Wah Chan, FRCP; Shun-Ling Kong, BN; Man-Oi Tang, BM; Jill Christensen, PhD; Robert W. Stadler, PhD; Chu-Pak Lau, MD, FRCP



Operation of algorithm for detecting decreases in impedance over time

Circulation. 2005;112:841-848

Intrathoracic Impedance Monitoring in Patients With Heart Failure

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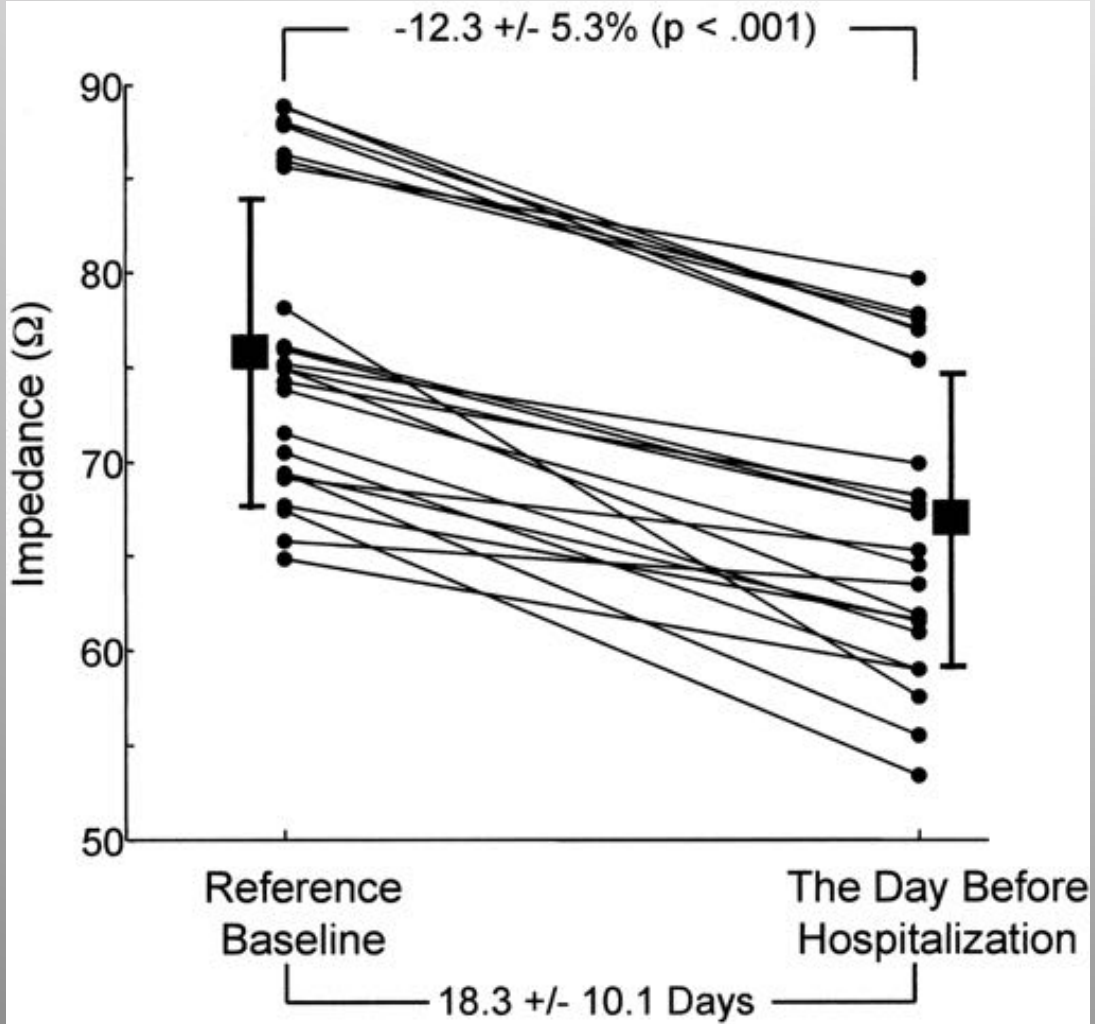


Comparison of intrathoracic impedance at reference baseline and 1 day before admission for 24 hospitalizations resulting from worsening heart failure in 9 patients.

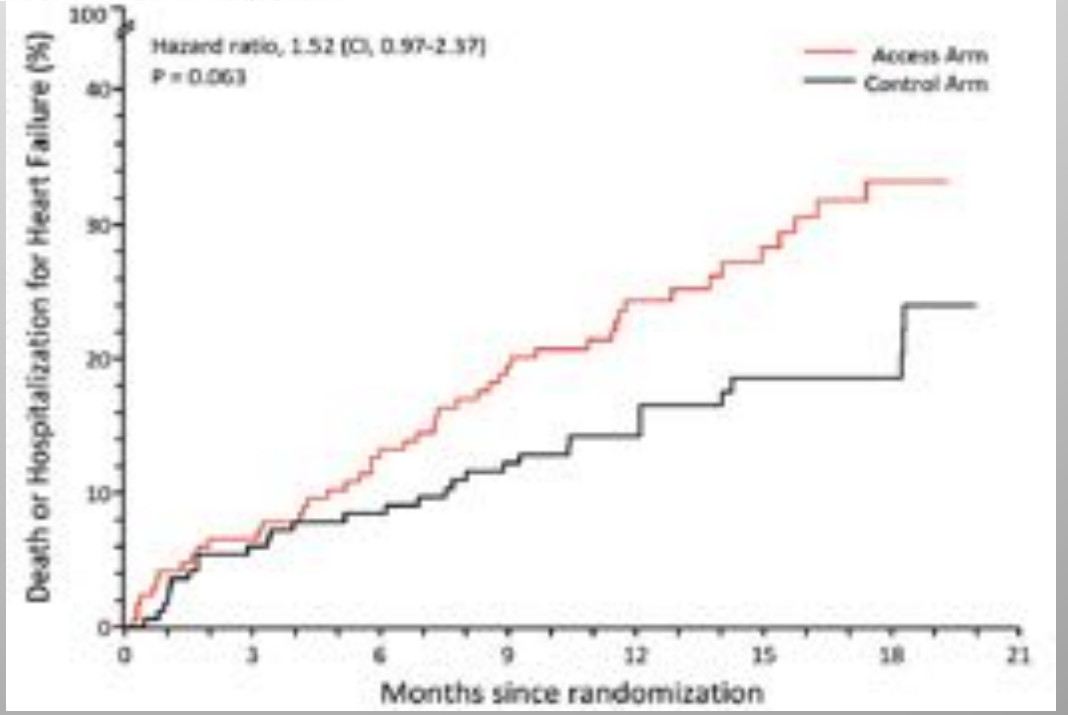
Circulation. 2005;112:841-848

Intrathoracic Impedance Monitoring, Audible Patient Alerts, and Outcome in Patients With Heart Failure

Dirk J. van Veldhuisen, MD; Frieder Braunschweig, MD; Viviane Conraads, MD; Ian Ford, PhD; Martin R. Cowie, MD; Guillaume Jondeau, MD; Josef Kautzner, MD; Roberto Muñoz Aguilera, MD; Maurizio Lunati, MD; Cheuk Man Yu, MD; Bart Gerritse, PhD; Martin Borggrefe, MD; for the DOT-HF Investigators

335 pts ICD/CRTD with OptiVol randomized

Primary endpoint was a composite of all-cause mortality and HF hospitalizations



Conclusion—Use of an implantable diagnostic tool to measure intrathoracic impedance with an audible patient alert did not improve outcome and increased heart failure hospitalizations and outpatient visits in heart failure patients.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT 00480077.

(***Circulation***. **2011;124:1719-1726.**)

Heart Failure 4

Telemedicine and remote management of patients with heart failure

Lancet 2011; 378: 731-39

Stefan D Anker, Friedrich Koehler, William T Abraham

	Recommender assessment frequency*	Methods of measurement
Non-invasive variables		
Systolic and diastolic blood pressure (mm HG)	Daily	By the patient (via device)
Pulse rate (beats per min)	Daily	By the patient (via device)
3-lead ECG	Daily	By the patient (via device), electrode placement needed
Systolic time intervals	Daily	By the patient (via ECG)
Heart-rate variability	Daily	By the patient (via ECG)
Bodyweight (kg)	Daily	By the patient (via device)
Blood glucose	Individually	By the patient (via device with blood sample)
Plasma concentrations of natriuretic peptides	Weekly-monthly	By the patient (via device with blood sample)
Oxygen saturation	In case of emergency	By the patient (via device)
Variables derived by acoustic cardiography	Daily	By the patient (via device)
Self-administered questions	Daily-monthly	By the patient (device-administered

Classification of HF Monitoring Systems

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- **Baseline/Cross-sectional predictors**
- **Longitudinal Predictors**

Baseline predictors:
Seattle Heart Failure Model (SHFM)

A number of predictive models are currently available stratifying the risk of wHF and death as functions of clinical and demographic characteristics.*

One of the most recent and accurate is the **SHFM**.**

It essentially receives clinical and demographic data as input :

- **Age and gender; NYHA Class; Ejection Fraction (LVEF)**
- **Ischemic aetiology; Systolic pressure**
- **Therapy (including implantable cardiac devices, PM, ICD, CRT)**
- **Haemoglobin, lymphocytes, uric acid, cholesterol, and serum sodium**

And returns a numerical score between -1 (best prognosis) and 4 (worst prognosis).

* Nutter AL, et al. Evaluation of 6 prognostic models used to calculate mortality rates in elderly heart failure patients with a fatal heart failure admission. Congest Heart Fail. 2010; 16(5):196-201

** Levy WC, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. Circulation. 2006; 113(11): 1424-1433.

Baseline predictors:
SHFM Model

- To calculate the **SHFM score**, each single variable is multiplied by its coefficient β (log odd ratio) as estimated from a 1125 patient cohort of the PRAISE1 trial.

$$\textbf{SHFM score} = \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_n x_n$$

- Once the score is computed, survival at time t (=1 year, 2 year, ...) is given by

$$\textbf{Survival}(t) = \exp[\lambda \times t \times \exp(\textbf{SHFM score})]$$

- **Where λ is 0.0405 /year as estimated with PRAISE1 cohort**

SHFM Model

Application of the Seattle Heart Failure Model in Patients on Cardiac Resynchronization Therapy

LAURA PERROTTA, M.D.,* GIUSEPPE RICCIARDI, M.D.,* PAOLO PIERAGNOLI, M.D.,* MARCO CHIOSTRI, M.D.,* GIULIA PONTECORBOLI, M.D.,* TIZIANA DE SANTO, M.S.,† FULVIO BELLOCCI, M.D.‡ NICOLA VITULANO, M.D.‡ MICHELE EMDIN, M.D.,§ GIOSUÈ MASCIOLI, M.D.,¶ ILARIA RICCERI, M.D.,* MARIA CRISTINA PORCIANI, M.D.,* ANTONIO MICHELUCCI, M.D.,* and LUIGI PADELETTI, M.D.*,¶

From the *University of Florence, Viale Morgagni, Florence, Italy; †Medtronic Italia, Rome, Italy; ‡Catholic University of Sacred Heart, Rome, Italy; §Fondazione Monasterio, Pisa, Italy; ¶Gavazzeni Hospital, Bergamo; Italy

Table III.

Discrimination and Calibration of SHFM for All-Cause Death/Transplant

	Predicted Survival (SE)	Observed Survival (SE)	C-statistic (95% CI)	H-L (P-Value)
1 year	89.5% (0.5%)	89.6% (1.7%)	0.70 (0.61–0.79)	3.83 (0.281)
2 years	81.0% (0.8%)	79.8% (2.4%)	0.69 (0.62–0.77)	4.31 (0.230)
5 years	62.4% (1.2%)	59.0% (4.2%)	0.69 (0.63–0.75)	2.10 (0.553)

SE = standard error; 95% CI = confidence interval at 95%; H-L = Hosmer–Lemeshow goodness-of-fit test.

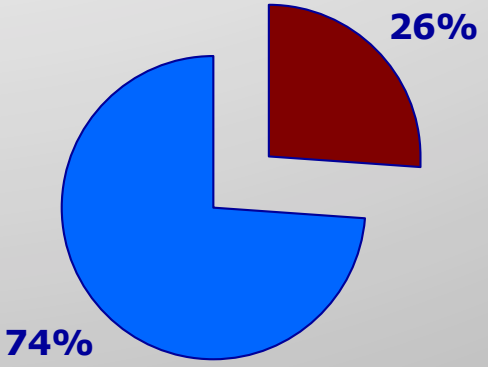
Pacing Clin Electrophysiol. 2011 Nov 6. doi: 10.1111/j.1540-8159.2011.03258.x. [Epub ahead of print]

Longitudinal Indicators

– Mean Heart Rate	⇨	– 1.8% increased risk of wHF per 1 bpm increase of mean heart rate
– Atrial Arrhythmias	⇨	– Well assessed predictor of wHF
– PVC frequency	⇨	– Associated with 5.5-fold increased risk of cardiovascular death
– Exercise and daily activity	⇨	– Inability to maximal exercise for at least 4 minutes predicts death and wHF
– Heart Rate variability	⇨	– HRV reduction is associated with wHF
– Thoracic Impedance	⇨	– 60% Positive Predictive Value

Longitudinal Indicators
Accuracy of HF prediction is still poor

- **Despite such long list of HF predictors, 7% to 26% of CRT patients are hospitalized for worsening Heart Failure (wHF) every year[1,2]**
- **This is mainly due to**
  - **Limited predictive value of single pieces of diagnostic information**
  - **Periodic, non-continuous monitoring of wHF indicators**



Proportion of patients hospitalized every year

1, Bristow MR, et al. Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure. N Engl J Med 2004; 350: 2140-2150.
2. Cleland JGF, et al. The Effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure. N Engl J Med 2005; 352: 1539-49

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ISSN 0735-1097/10/$36.00
doi:10.1016/j.jacc.2009.11.089

QUARTERLY FOCUS ISSUE: HEART FAILURE

Combined Heart Failure Device Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalizations

Results From PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) Study

David J. Whellan, MD, MHS,* Kevin T. Ousdigian, MSEE, MSIE,† Sana M. Al-Khatib, MD, MHS,‡ Wenji Pu, PHD,† Shantanu Sarkar, PHD,† Charles B. Porter, MD,§ Behzad B. Pavri, MD,* Christopher M. O'Connor, MD,‡ for the PARTNERS Study Investigators

Philadelphia, Pennsylvania; Minneapolis, Minnesota; Durham, North Carolina; and Kansas City, Kansas

Prospective, multicenter study in patients receiving cardiac resynchronization therapy (CRT) implantable cardioverter-defibrillators (694 pts, FU 12 months) evaluating the ability of combined HF device diagnostics to dynamically risk-stratify patients for HF events over set time intervals

Partners Study

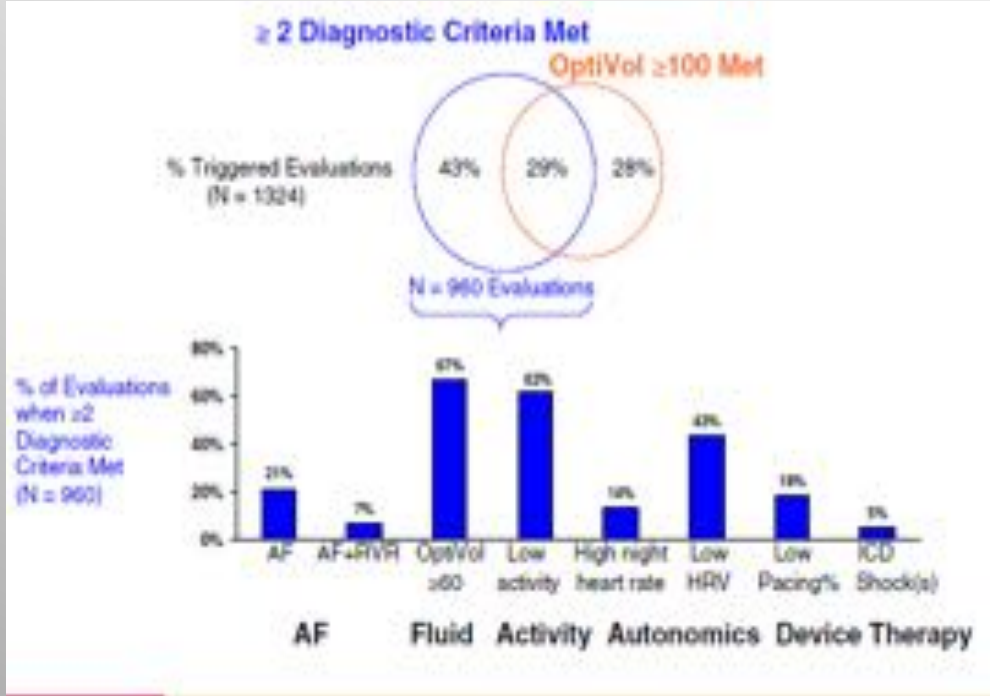


Figure 2 Combined HF Device Diagnostics Triggered

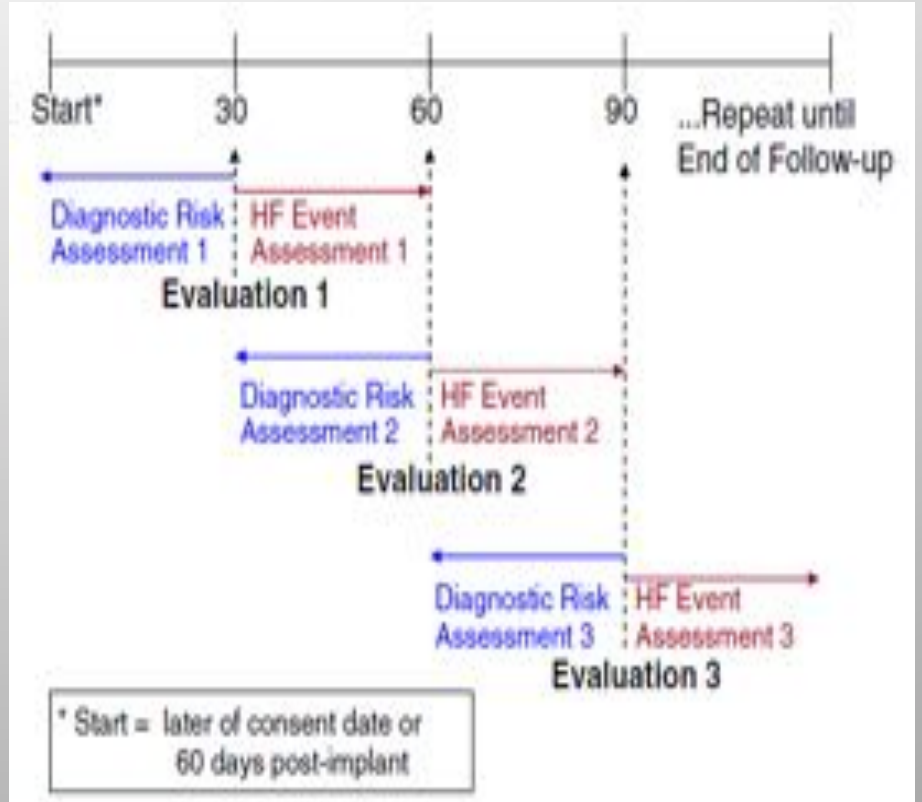


Figure 1 Monthly Review Model

Every 30 days the previous 30 days are evaluated for heart failure (HF) device diagnostic risk and then the subsequent 30 days are evaluated for HF event risk.

Diagnostic Risk Assessment: the algorithm was considered positive if a patient had 2 of the following abnormal criteria during a 1-month period

Partners: Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients with HF; D.J. Whellan (Department of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania)

Partners Study

Patients with a combined HF diagnostic algorithm had 5.5 fold ↑risk of HF event within 30 days

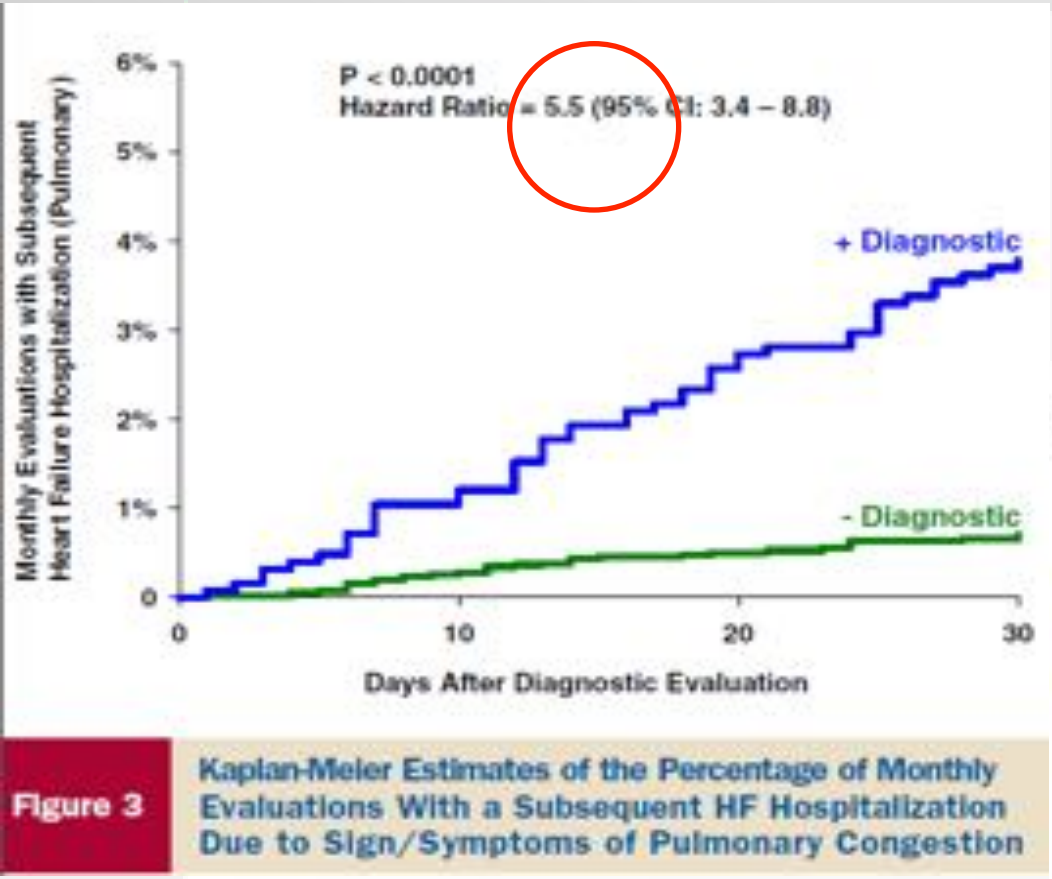
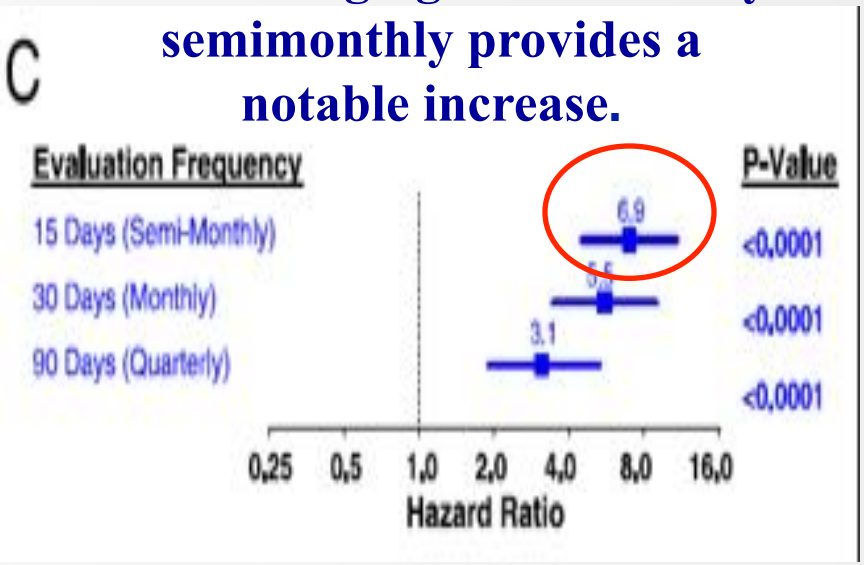


Figure 3 Kaplan-Meier Estimates of the Percentage of Monthly Evaluations With a Subsequent HF Hospitalization Due to Sign/Symptoms of Pulmonary Congestion

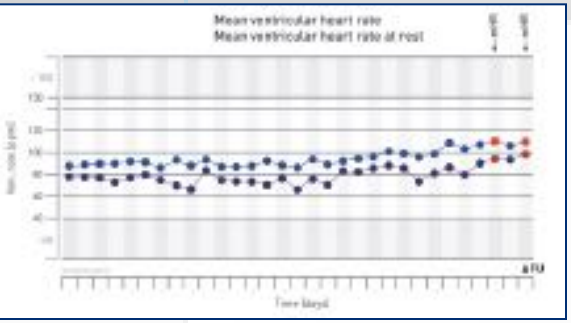
Increasing the frequency of reviewing the HF device diagnostics from quarterly to monthly will substantially increase the ability to identify patients at higher risk, whereas changing from monthly to semimonthly provides a notable increase.



Partners: Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients with HF; D.J. Whellan (Department of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania)

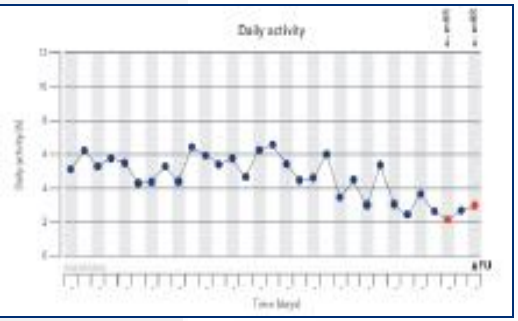
Home Monitoring®
parameters predictors of heart failure

Current remote monitoring technology (Home Monitoring) allows daily sampling of most longitudinal predictors

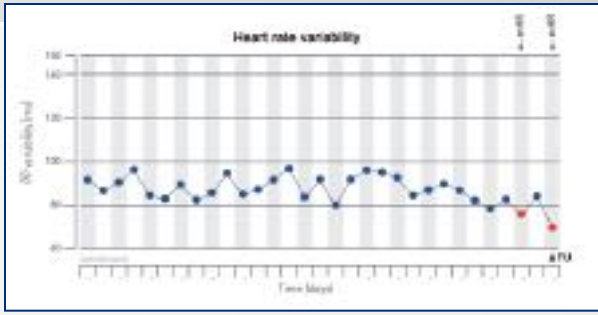


Mean ventricular HR and mean ventricular HR at rest

Level of activities



AF Burden



Heart Rate Variability

% CRT stimulation

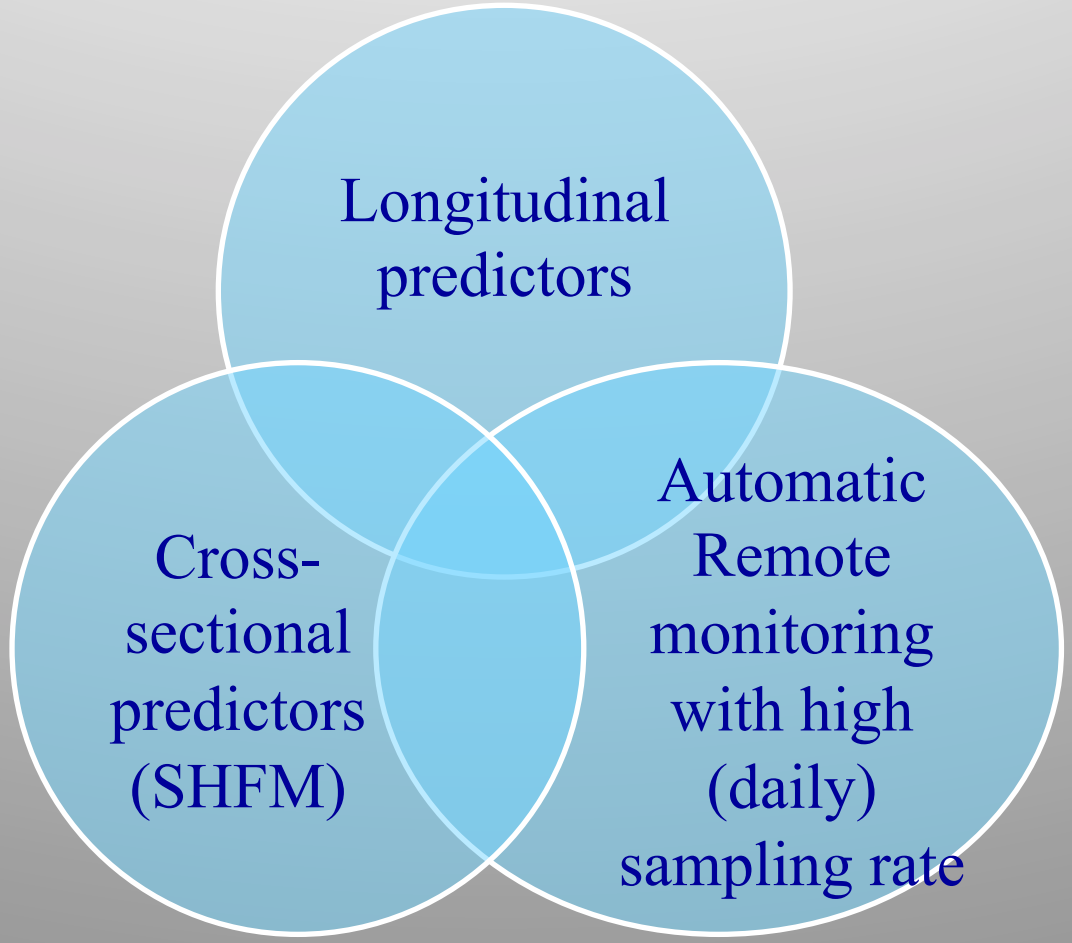
Left ventricular capture

VPB /h

Pulmonary fluid accumulation sensor

Combining predictors and highly performing Remote Monitoring

- **The key to success lies in the combinations of**



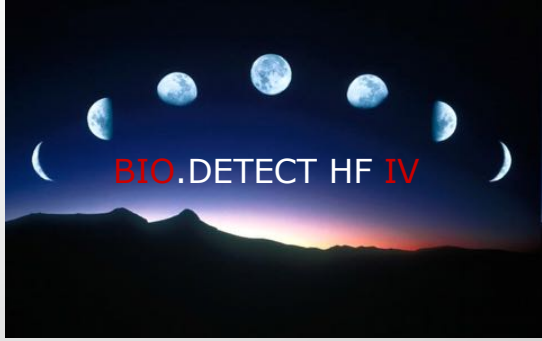
SELENE HF

Selection of potential predictors of worsening Heart Failure

SELENE HF

Sample size and study duration

- **Event-driven Study, collecting 50 primary endpoint events**
- **625 subjects to enroll, including dropouts**
- **enrollment period: of 3 years**
- **overall study duration: 4 years (expected mean follow-up period: 1 year).**



SELENE HF
Objectives

- **Primary endpoint**
  - ***First HF-related hospitalization***
- **Secondary endpoint**
  - **A composite of**
    - ***death for worsening HF,***
    - ***hospitalizations for worsening HF,***
    - ***acute interventions for worsening HF.***

SELENE HF

Inclusion Criteria

- Subjects who have already received and ICD and/or CRT-D therapy within 12 months before study participation
- LVEF ≤ 35%;
- NYHA Class II or III Heart Failure;
- Men and women 18 years of age or older;
- Understand the nature of the procedure;
- Give written informed consent

SELENE HF

Exclusion Criteria

- No indication or contraindication for ICD or CRT-D therapy;
- Permanent AF;
- NYHA Class IV Heart Failure;
- Subjects with irreversible brain damage from preexisting cerebral disease;
- Subjects with acutely decompensated heart failure;
- Expected heart transplantation within next six months or planned cardiac surgery within next 3 months, or life expectancy less than six months.
- Unstable geographical residence and/or GSM-free residence;

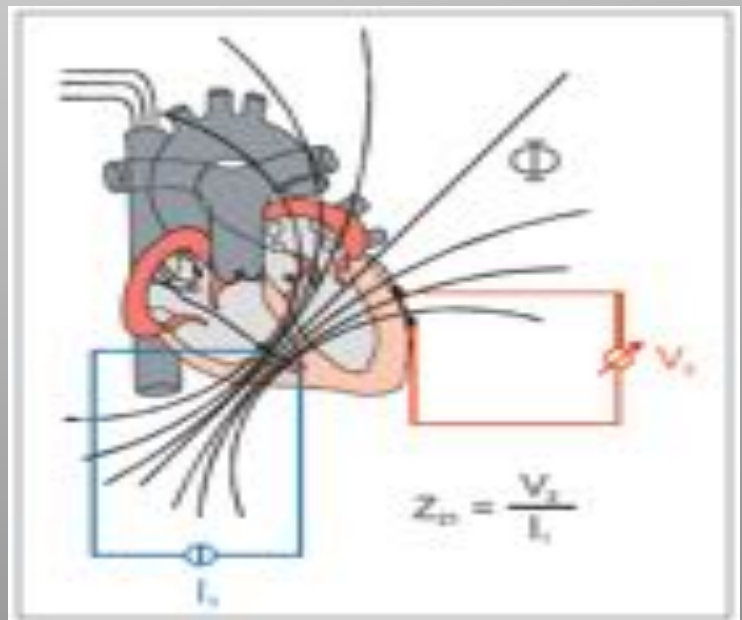
SELENE HF
Study procedures

- Patients will be stratified according the baseline indexes (SHFM score)
- wHF hospitalizations will be documented
- HF monitor trends will be correlated with wHF hospitalization episodes
- Remote Monitoring trends related wHF will be blinded to Investigators but collected by nurses

SELENE HF
IntraCardiac Impedance

Future HF Hemodynamic sensors

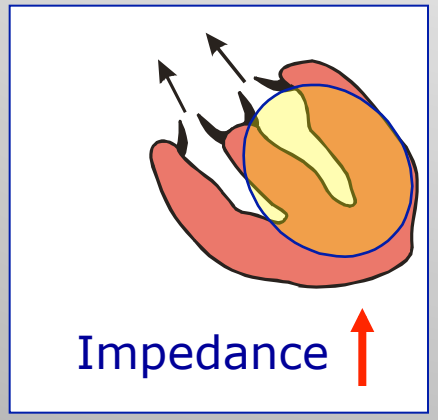
– **The intracardiac impedance is directly correlated with hemodynamics and has been implemented in new generation CRT-D devices**



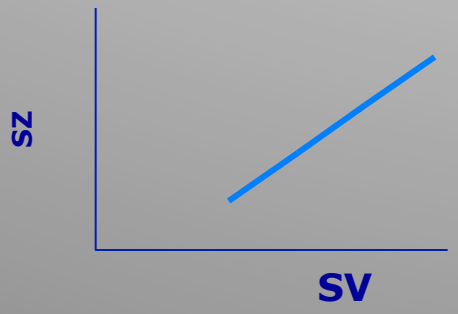
SELENE HF

Future HF Hemodynamic sensors

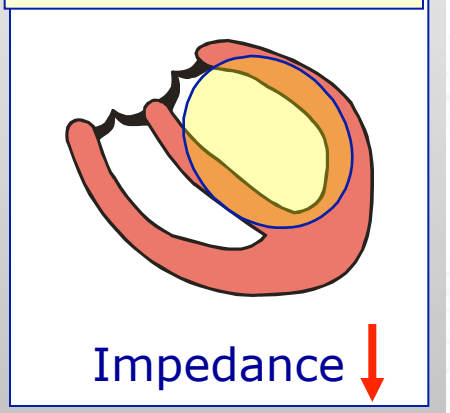
Systole



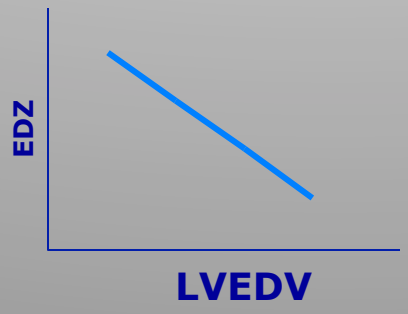
Positive correlation between impedance and systolic volume

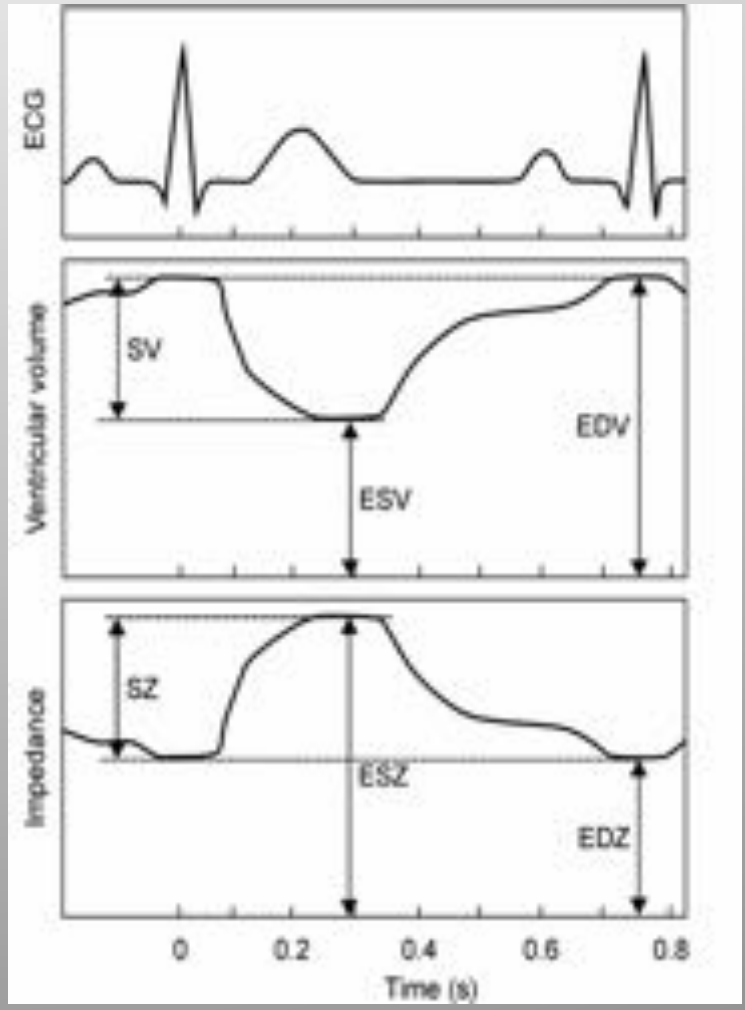


Diastole



Inverse correlation between impedance and diastolic volume





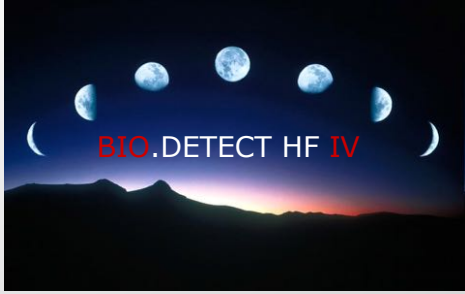
Studio SELENE HF

Selection of potential predictors of worsening Heart Failure.

- **Steering Committee**
  - G. Botto, Como
  - L. Calò, E. De Ruvo, Roma
  - Maria Rosa Costanzo, Neperville IL (US)
  - A. Curnis, L. Bontempi, Brescia
  - A. D'Onofrio, Napoli
  - E. Gronda, Milano
  - L. Padeletti, Firenze
  - R. Ricci, Roma
  - G. Sinagra, M. Zecchin, Trieste
  - A. Vado, Cuneo
  - G. Zanotto, Legnago

- **Adverse Event Advisory Board**

Adverse Event Advisory Board (AEAB)



AEAB members :

Giuseppe Boriani, Bologna, chairman

Emanuele Bertaglia, Padova, primary adjudicator

Ennio Pisanò, Lecce, primary adjudicator

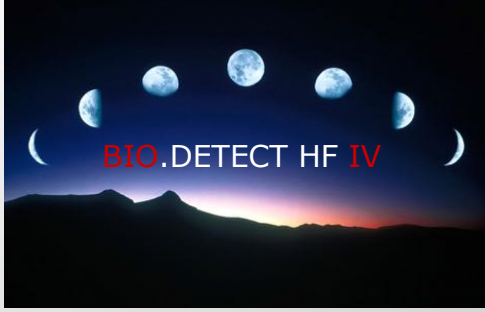
AEAB responsibility:

AEAB is in charge of adjudicating (serious) adverse events which are associated with the following primary and secondary endpoints:

Primary endpoint: first HF-related hospitalization

Secondary endpoint: a composite of death for worsening HF, hospitalizations for worsening HF, acute interventions for worsening HF.

Selene HF Study
Analysis purpose

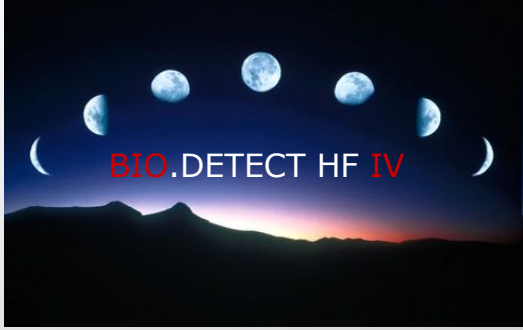


- A multivariate logistic analysis will be implemented modelling the log-odd-ratio of *first HF hospitalizations* as a function of proper transformations (f_k) of the HM variables, and adjusting with the baseline characteristics (SHFM score).

- HF Monitor trends will be blinded to Investigators and to Event Adjudication Board.

- HF remote Monitor Trends will be reviewed and analyzed off-line basing on a Varying Time Windows Model

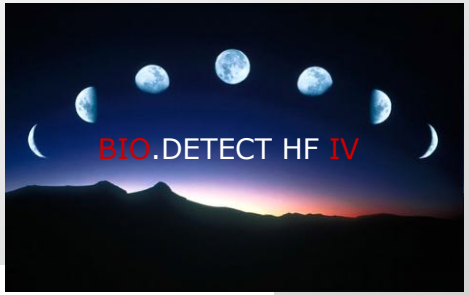
Logistic model in Selene HF Study

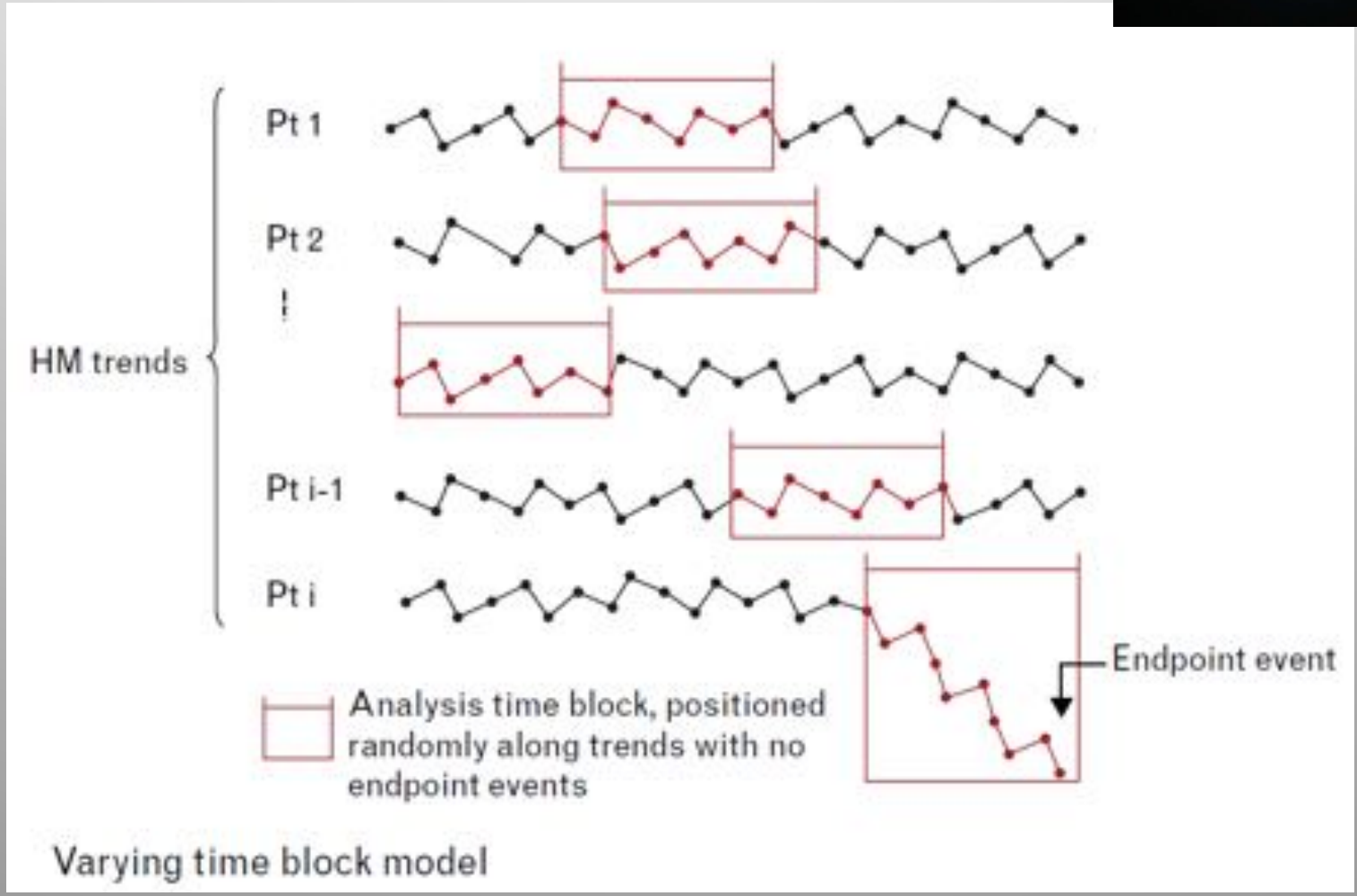


$$\ln\left(\frac{P}{1-P}\right) = \alpha + \beta_1 f_1(x_1) + \beta_2 f_2(x_2) + \ldots + \beta_{11} f_{11}(x_{11}) + \gamma_{SHFM} x_{SHFM}$$

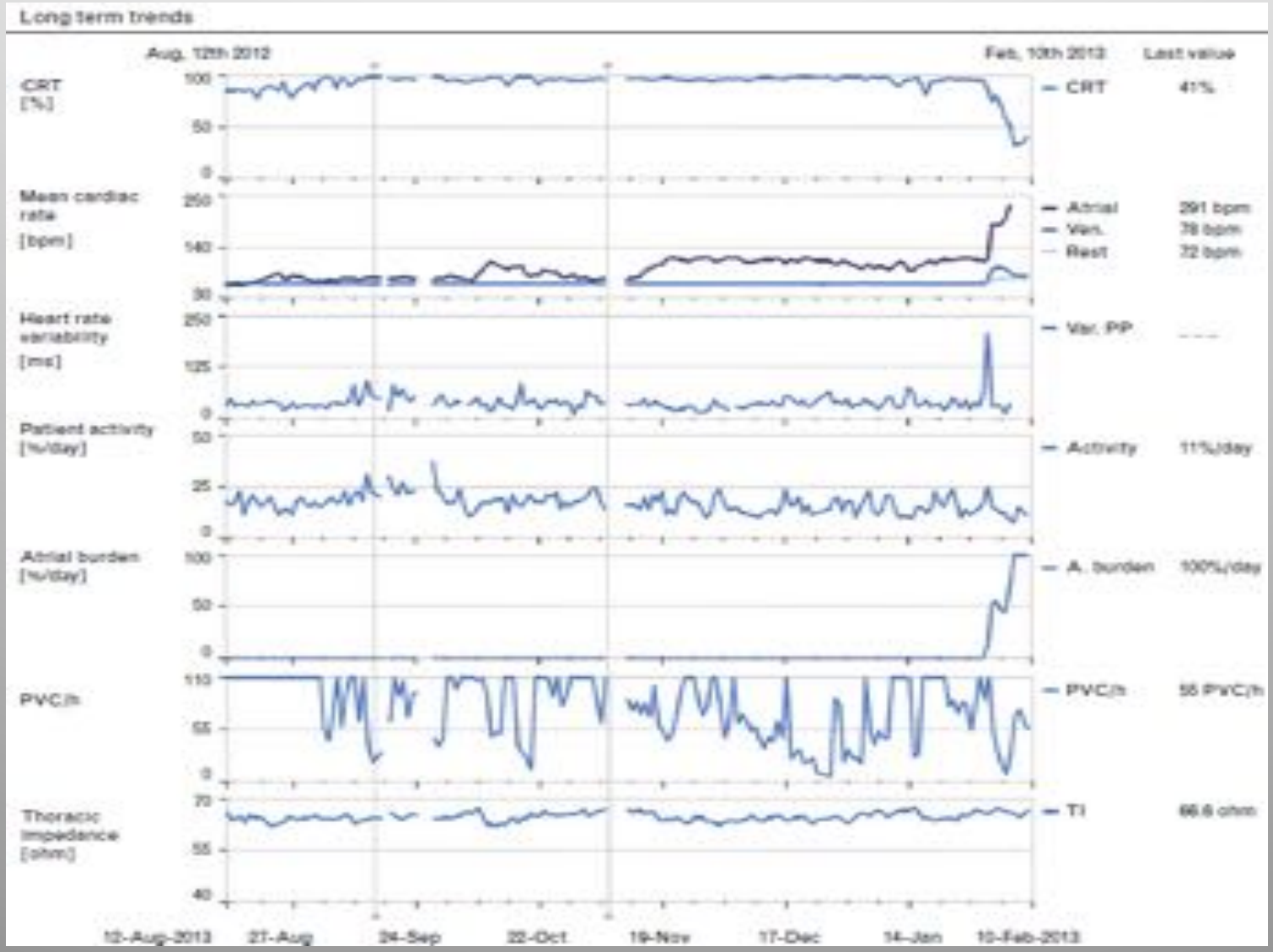
- where
  - P is the probability of the primary endpoint event (first wHF-related hospitalization)
  - x_k HF Monitor variables (mean heart rate, daily activity, AF burden, etc.)
  - f_k suitable transformations to be applied during analysis
  - α, β_k, γ_{SHFM} regression coefficient estimating the log odd ratios associated with each covariate.

Time window model



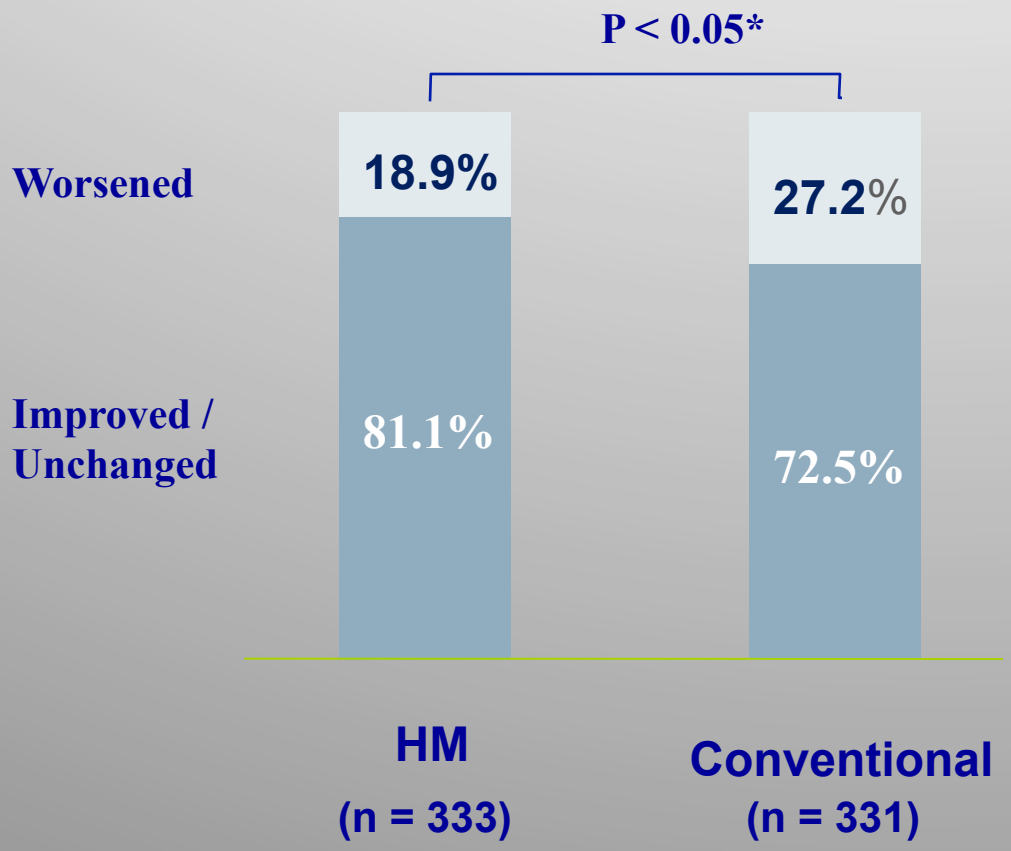


Home Monitoring trends of HF related variables



Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial

Gerhard Hindricks, Milos Taborsky, Michael Glikson, Ullus Heinrich, Burghard Schumacher, Amos Katz, Johannes Brachmann, Thorsten Lewalter, Andreas Goette, Michael Block, Josef Kautzner, Stefan Sack, Daniela Husser, Christopher Piorkowski, Peter Søgaard, for the IN-TIME study group*



Reduction of worsening of clinical status

Lancet 2014; 384:583-90

Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial

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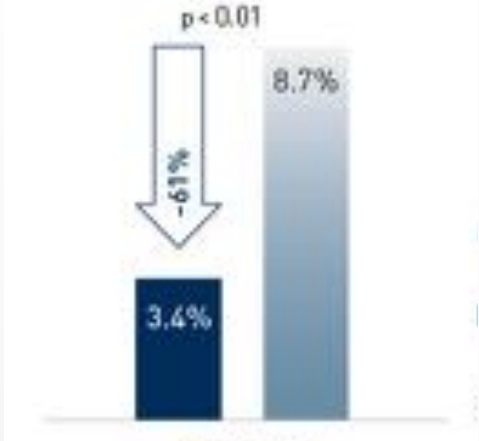
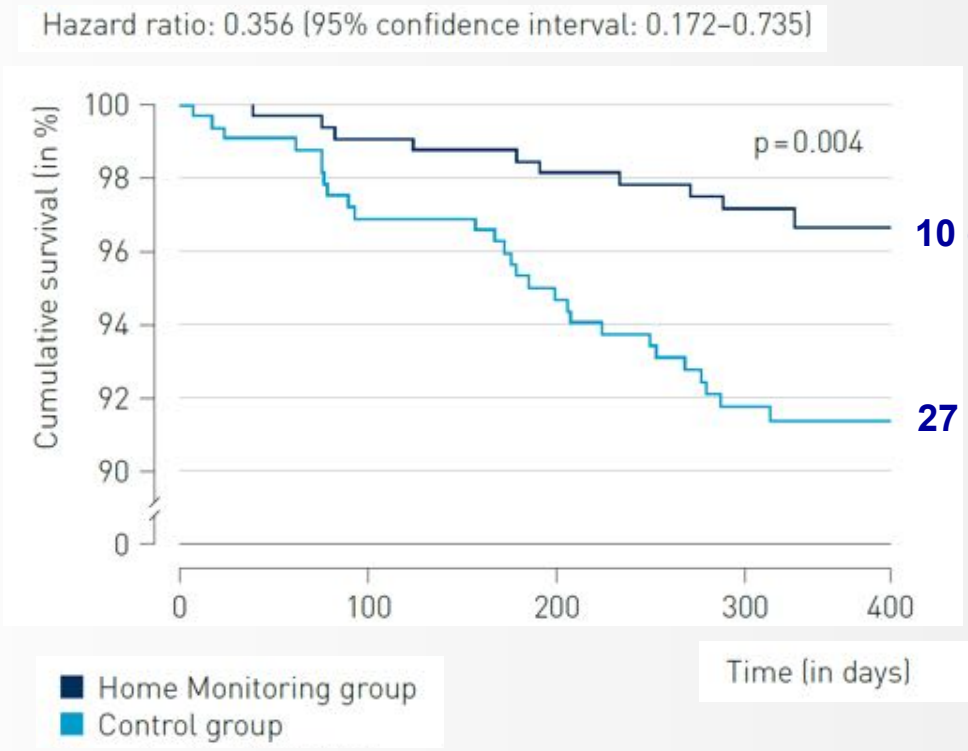


all-cause Mortality after 12 months



10 deaths (3.4%)

27 deaths (8.7%)

Lancet 2014; 384: 583–90

Conclusions

- **Remote control is becoming part of routine HF patient follow-up management.**
- **The clinical benefit of RM on HF treatment is the objective of current research.**
- **Several HF-related indexes are currently available remotely on daily basis but an isolated piece of information have a limited predictive value**
- **A proper combination of more variables and their 24-hour sampling may allow developing a combined HM diagnostic algorithm to effectively predict HF worsening within given time windows.**

Conclusions

- **Large prospective trials are needed to achieve this objective**
- **The upcoming Selene HF Study will be a large prospective trial combining several cross-sectional and longitudinal HF predictors with current Remote Monitoring technology.**

Heart failure and CRT : new topics and evidence in 2015

The integrated approach of multiple parameters to monitor the HF worsening

Antonio D'Onofrio, MD, FANMCO, FESC

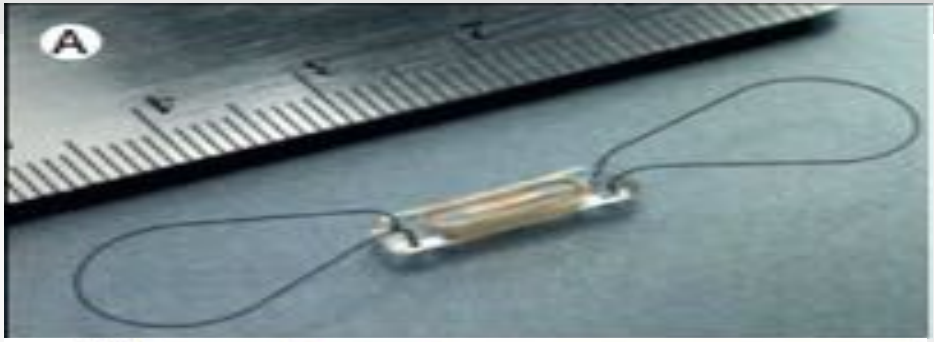
Dipartimento di Cardiologia

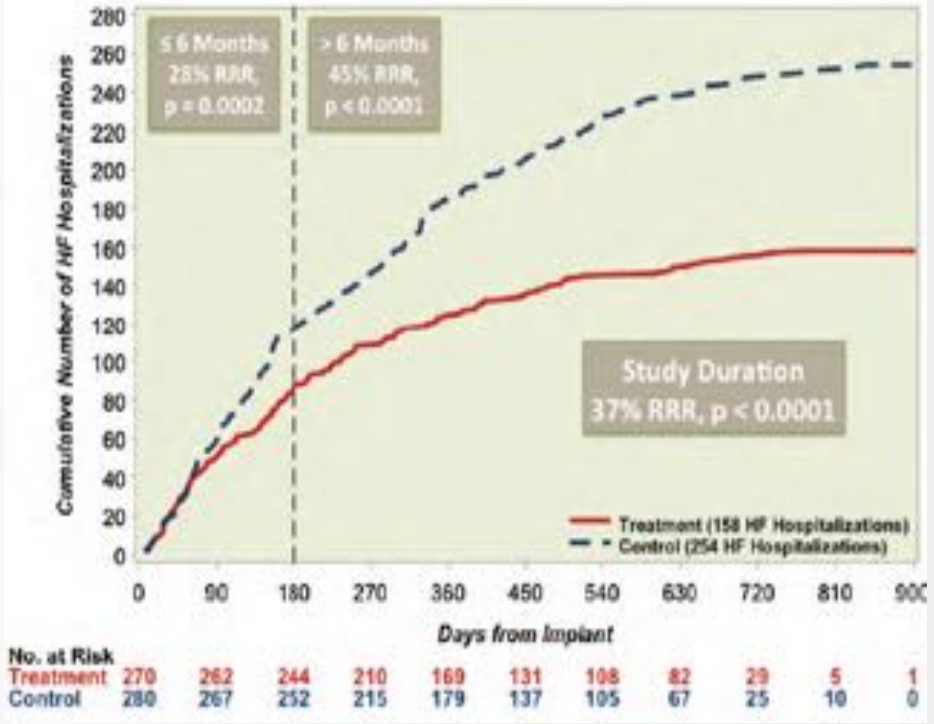
UOSD di Elettrofisiologia, Studio e Terapia delle Aritmie

AORN "Dei Colli – Osp. V. Monaldi"

Invasive Monitoring

- **The use of pulmonary artery pressure measurement system has been shown to significantly reduce risk of heart failure hospitalization in a large randomized controlled study (CHAMPION)**





Abraham WT et al. *Lancet*, 2011; 377: 658-666_CHAMPION Trial

Baseline predictors:
Seattle Heart Failure Model SHFM

A number of predictive models are currently available stratifying the risk of wHF and death as functions of clinical and demographic characteristics.*

One of the most recent and accurate is the **SHFM**.**

It essentially receives clinical and demographic data as input :

- Age and gender
- NYHA Class
- Ejection Fraction (LVEF)
- Ischemic aetiology
- Systolic pressure
- Therapy (including implantable cardiac devices, PM, ICD, CRT)
- Haemoglobin, lymphocytes, uric acid, cholesterol, and serum sodium

And returns a numerical score between -1 (best prognosis) and 4 (worst prognosis).

* Nutter AL, et al. Evaluation of 6 prognostic models used to calculate mortality rates in elderly heart failure patients with a fatal heart failure admission. Congest Heart Fail. 2010; 16(5):196-201

** Levy WC, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. Circulation. 2006; 113(11): 1424-1433.

Classification of HF Monitoring Systems

HF Monitoring Systems

- **Invasive Systems**
- **Non-Invasive Systems**

- **Baseline/Cross-sectional predictors**
- **Longitudinal Predictors**

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QUARTERLY FOCUS ISSUE: HEART FAILURE

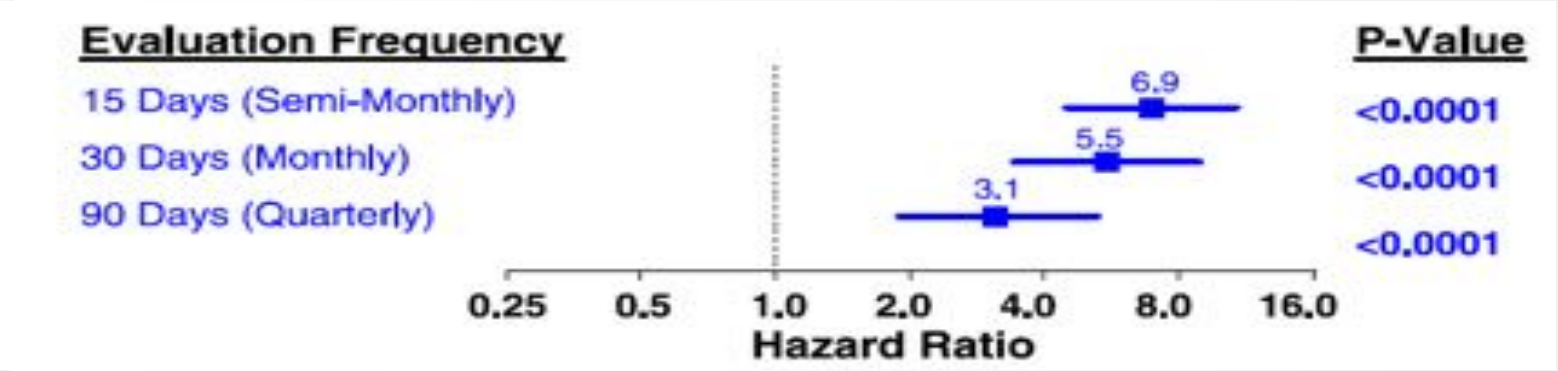
Combined Heart Failure Device Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalizations

Results From PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) Study

David J. Whellan, MD, MHS,* Kevin T. Ousdigian, MSEE, MSIE,† Sana M. Al-Khatib, MD, MHS,‡ Wenji Pu, PhD,† Shantanu Sarkar, PhD,† Charles B. Porter, MD,§ Behzad B. Pavri, MD,* Christopher M. O'Connor, MD,‡ for the PARTNERS Study Investigators

Philadelphia, Pennsylvania; Minneapolis, Minnesota; Durham, North Carolina; and Kansas City, Kansas

- Whellan et al. (2010) showed that
  - Combining more longitudinal predictors and
  - Within narrow evaluation periods
- Predictive power remarkably increases



* Whellan DJ, et al. Combined heart failure device diagnostics identify patients at higher risk of subsequent heart failure hospitalizations: results from PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) study. J Am Coll Cardiol. 2010; 55(17): 1803-10.

- **Advances in telecommunication technologies have created new opportunities to provide telemedical care as an adjunct to medical management of patients with heart failure.**
- **The mainstay of telemedicine is early detection of disease deterioration and prompt medical intervention.**
- **The key to success of this approach is the predictive value of the monitored variables.**

Invasive Monitoring

- **Implantable cardiac devices with telemedical features can remotely monitor**
  - **device function and usage in heart failure,**
  - **ICD shocks and status of batteries**
  - **changes in various physiological variables, such as heart rate, heart rate variability, atrial fibrillation, physical activity…**

Telemonitoring of HF: misleading messages

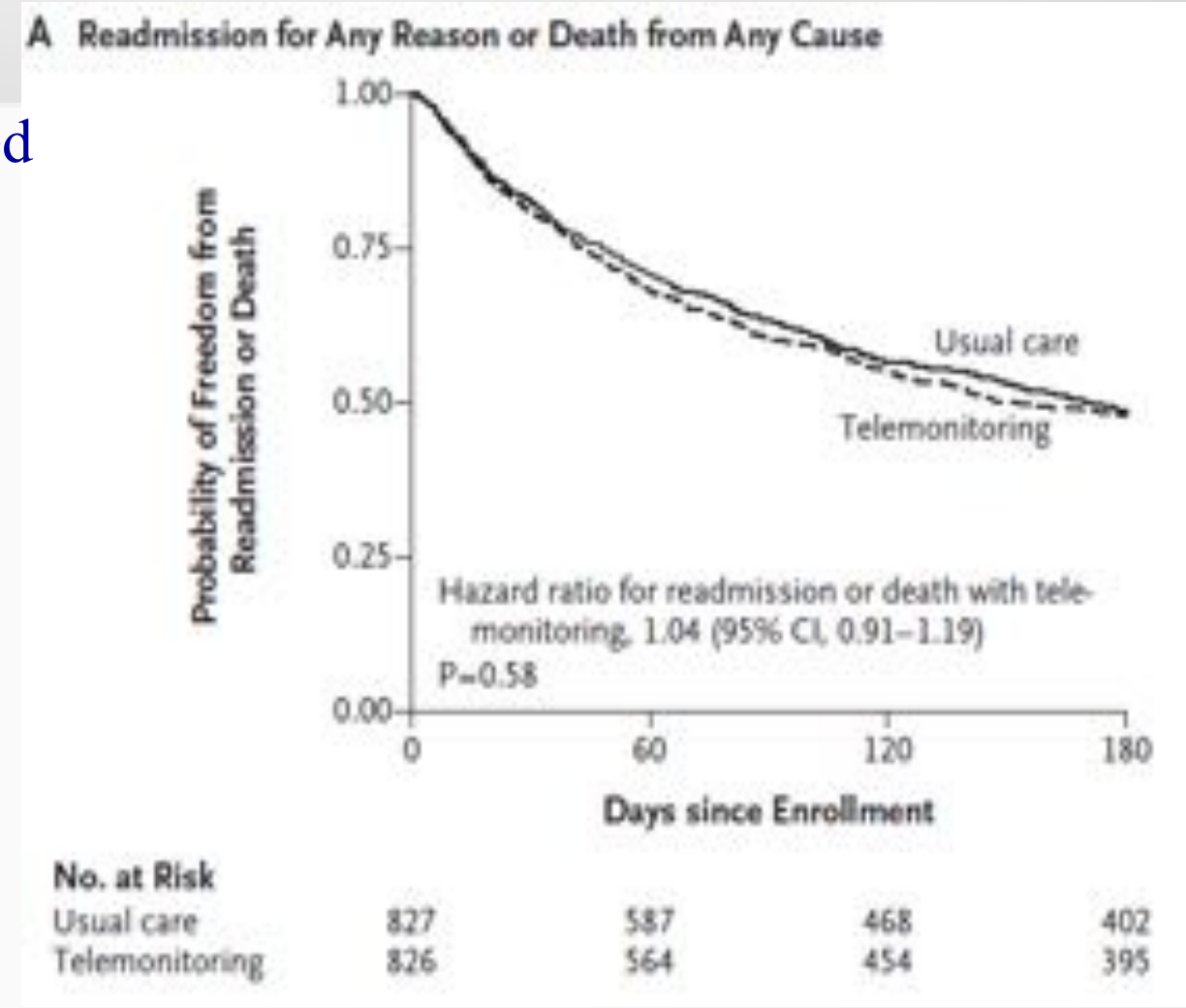
Telemonitoring in Patients with Heart Failure

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.

New Engl J Med 2010; 363: 2301-2309

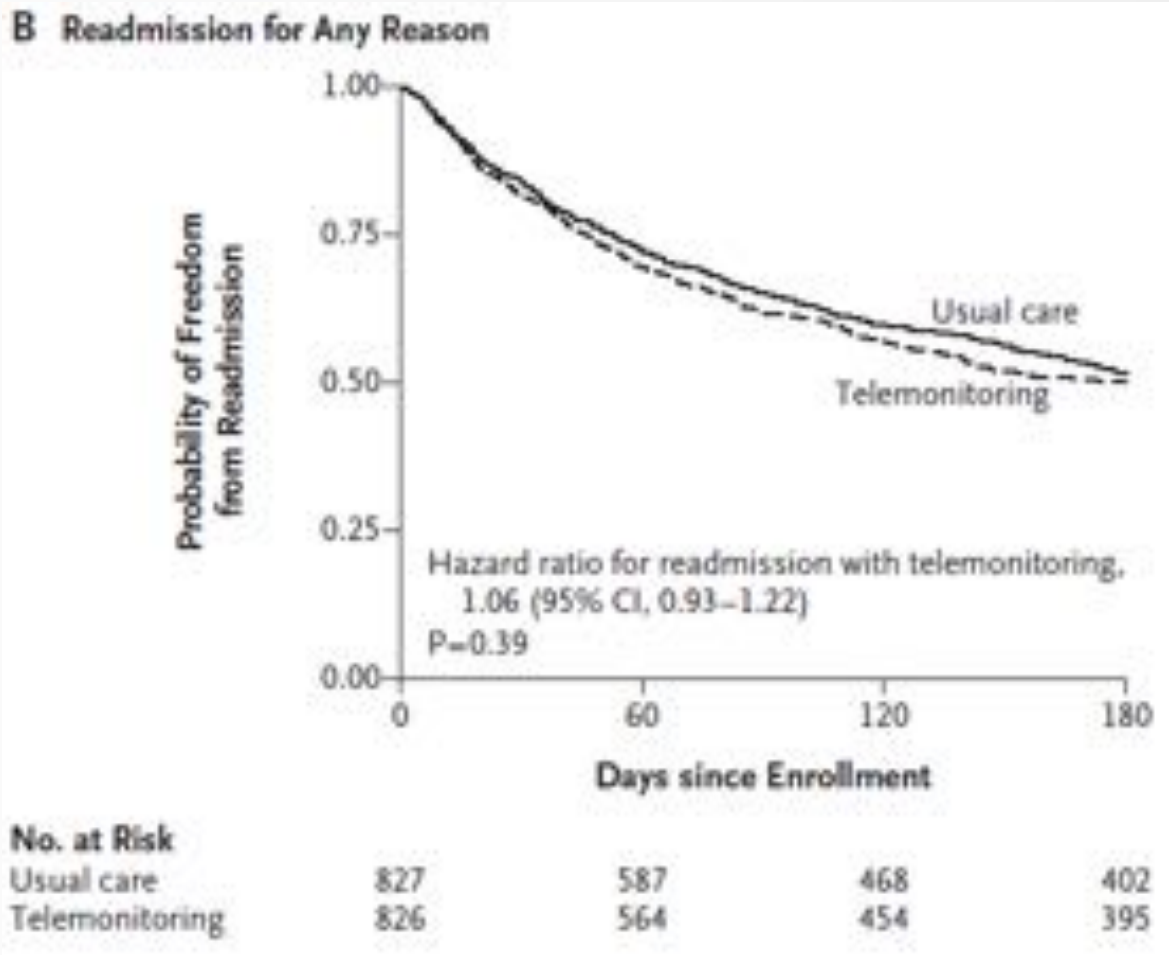
Telemonitoring of HF: misleading messages

1653 patients were enrolled from 2006 through 2009



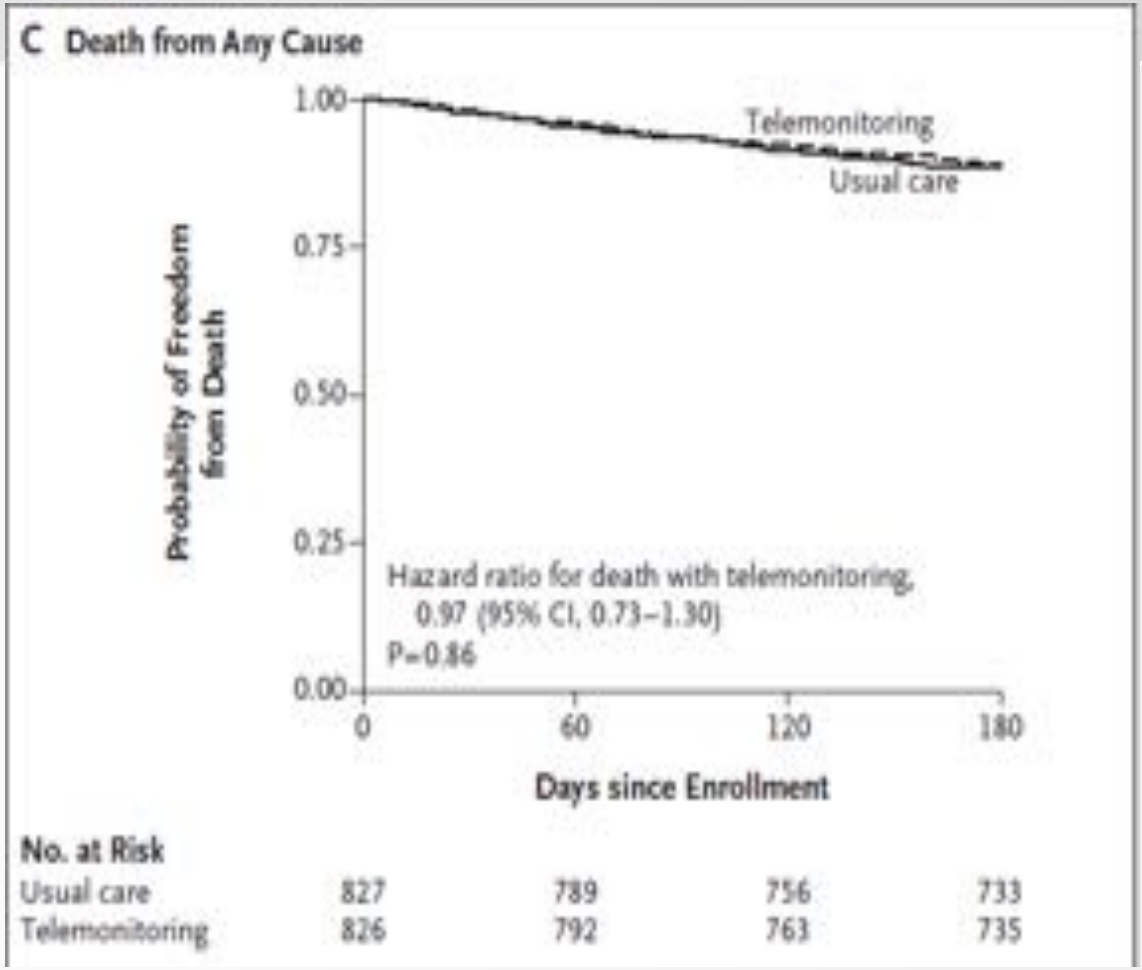
Chadhry SI, et al.
New Engl J Med
2010; 363: 2301-2309

Telemonitoring of HF: misleading messages



Chadhry SI, et al. New Engl J Med 2010; 363: 2301-2309

Telemonitoring of HF: misleading messages



Chadhry SI, et al.
New Engl J Med
2010; 363: 2301-2309

Telemonitoring of HF: misleading messages

We found no reduction in the risk of readmission or death from any cause with telemonitoring as compared with usual care

There were no reductions in the risk of hospitalization for heart failure, the number of days in the hospital, or the time to readmission or death

In summary, a telemonitoring strategy failed to provide a benefit over usual care in a setting optimized for its use.

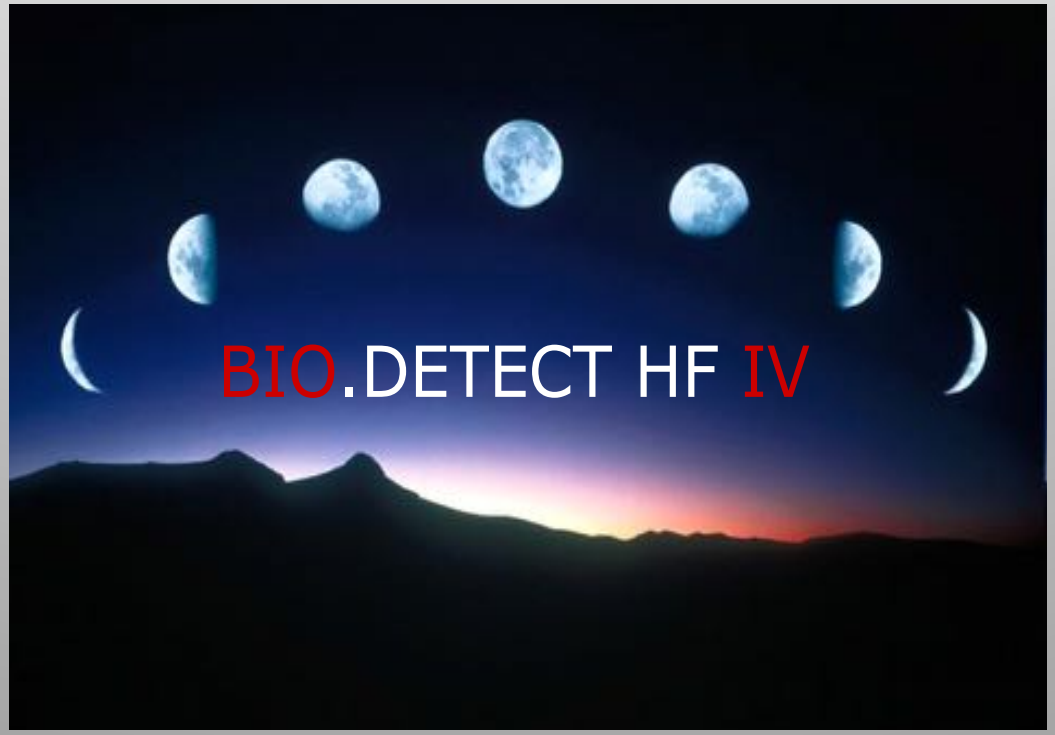
Monitoring parameters predictors of heart failure

- **% stimulation CRT**: monitors the delivery of CRT therapy
- **HR Variability** : information about the neurohumoral status
- **Mean ventricular rate and PVC/h**: predictor of hospitalization and mortality [1-4]
- **AF Burden**: quickly identifies this dangerous co-morbidities [5-6]
- **Level activities**: identifying the patient's activity and the quality of life

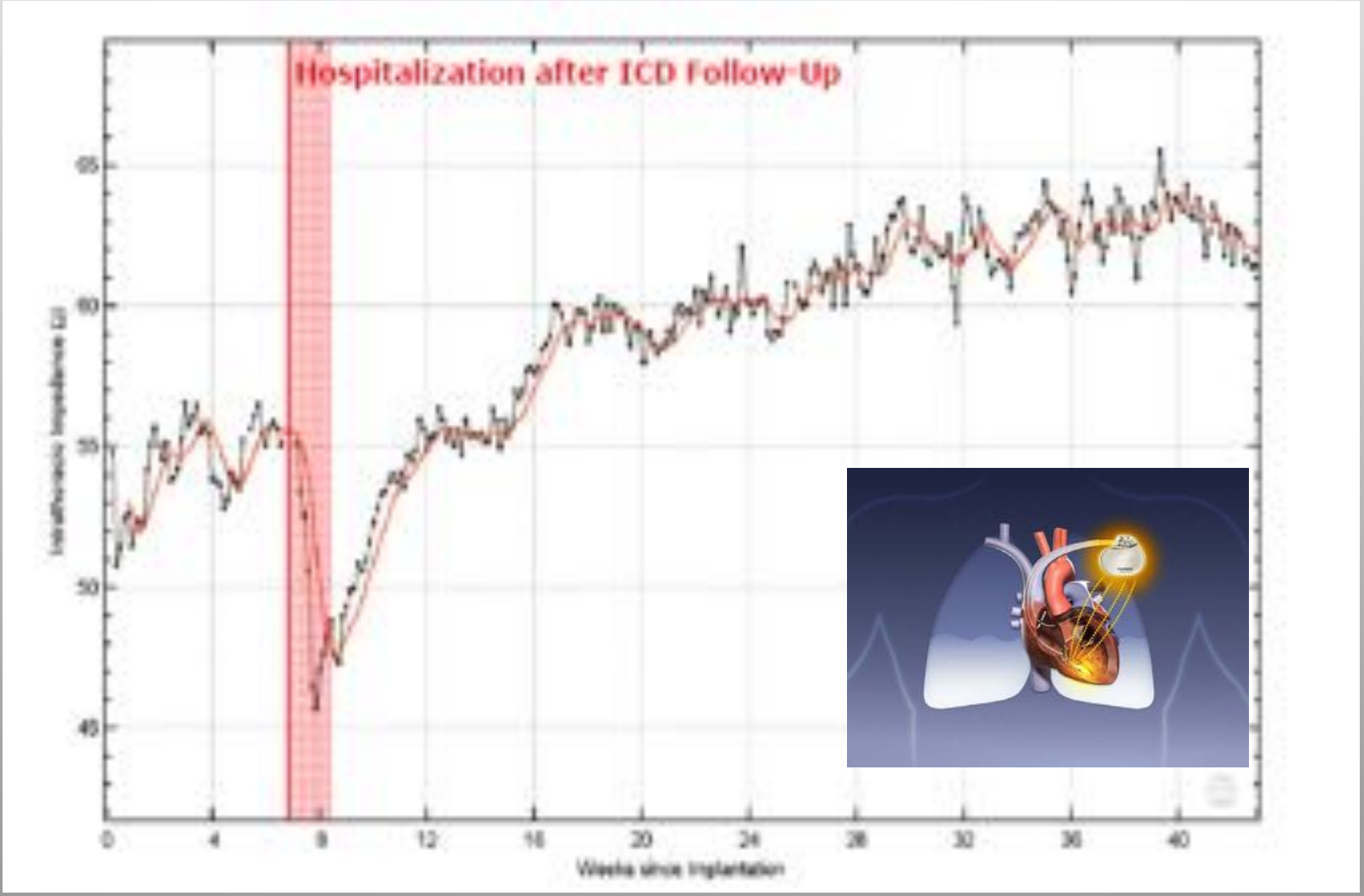
1) Lechat P. et al, Circulation. 1997 Oct 7; 96 (7): 2197–205.
2) Kannel WB. et al, Am Heart J. 1987 Jun; 113 (6): 1489–94.
3) Lechat P. et al, Circulation. 2001 Mar 13; 103 (10): 1428–33.
4) Madsen BK. et al, Int J Cardiol. 1997 Jan 31; 58 (2): 151–62.
5) Opasich C. et al, Am J Cardiol. 2001 Aug 15; 88 (4): 382–7.
6) Middlekauff HR. et al, Circulation. 1991 Jul; 84 (1): 40–8.

SELENE HF

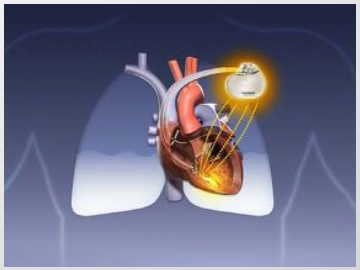
Thoracic Impedance



Intrathoracic impedance



Intrathoracic impedance



- **Despite IT has been estimated 60% sensitive with poor specificity, it may be an important wHF predictor if combined with other indexes and with 24-hour sampling RM trasmissions.**

*Vollmann D, Eur Heart J 2007

Bio.Detect HF IV
Objectives

- Primary endpoint

  First HF-related hospitalization

- Secondary endpoint

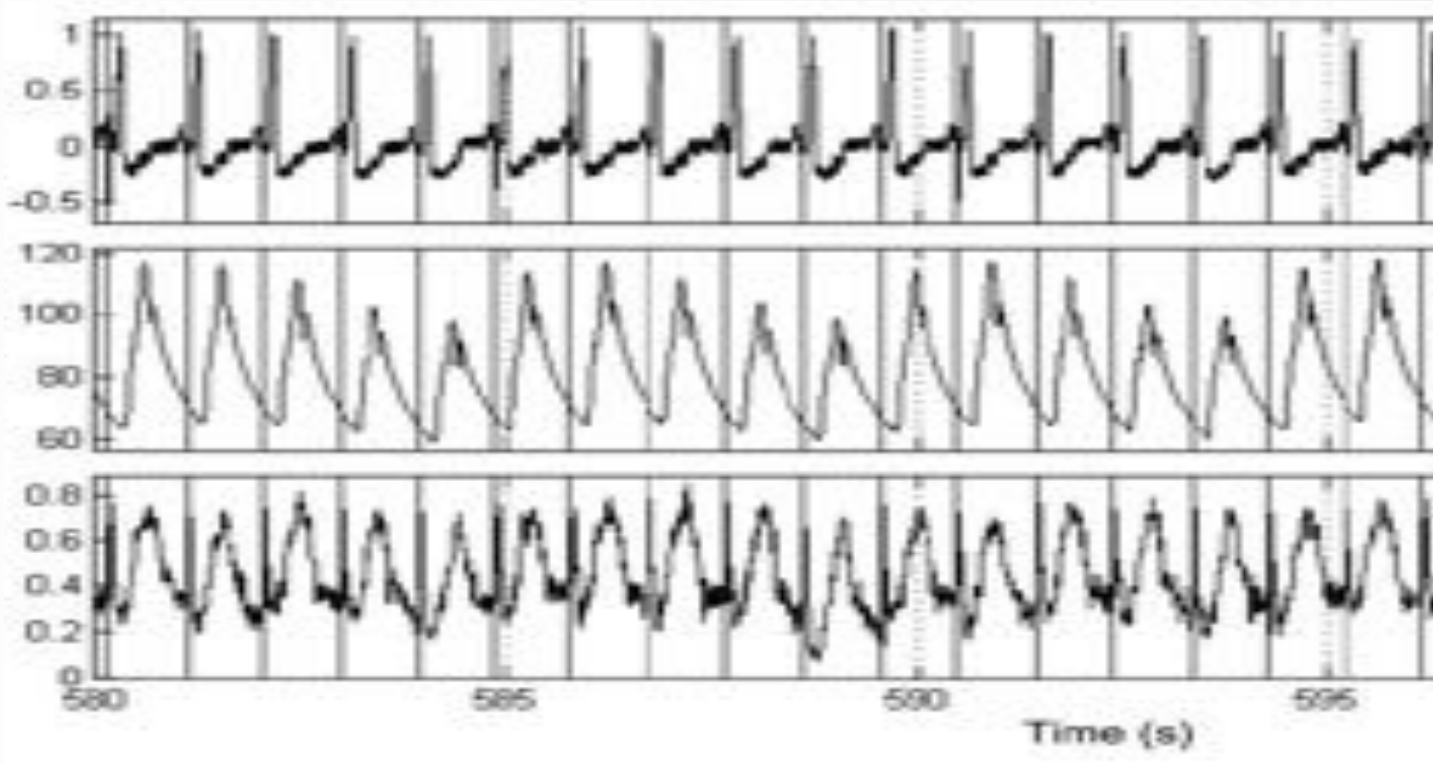
  A composite of death for worsening HF,
  hospitalizations for worsening HF,
  acute interventions for worsening HF.

Impedance and stroke volume correlation $r = 0.82 \pm 0.16$*

ECG

Aorta Pressure

Impedance signal



*Bocchiardo M, Europace, 2010

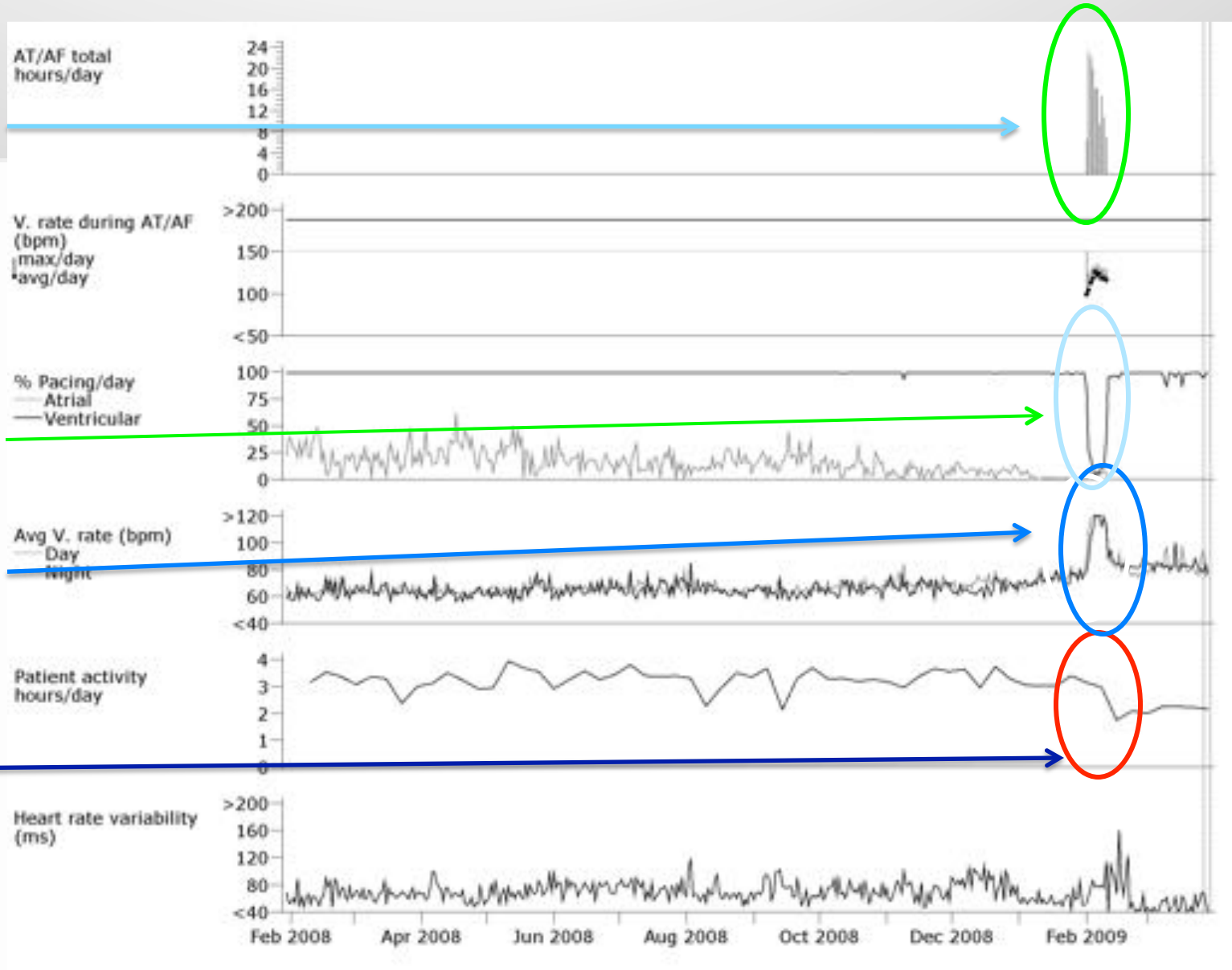
AF induced HF

AT/AF

↓ % CRT

Day and Night HR increase

↓ Patient Activity



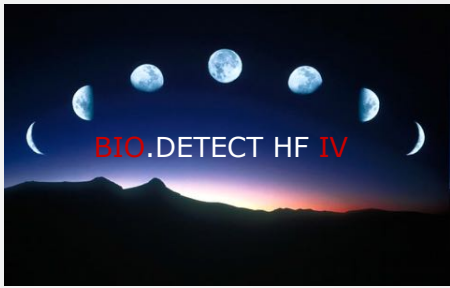
Bio.Detect HF IV-SELENE HF Study. Objective

Patients will be stratified according the baseline indexes (SHFM score)

Remote Monitoring trends related HF Monitor trends will be blinded to Investigators and collected.

wHF hospitalizations will be documented

HF monitor trends will be correlated with wHF hospitalization episodes



Inclusion Criteria

Inclusion

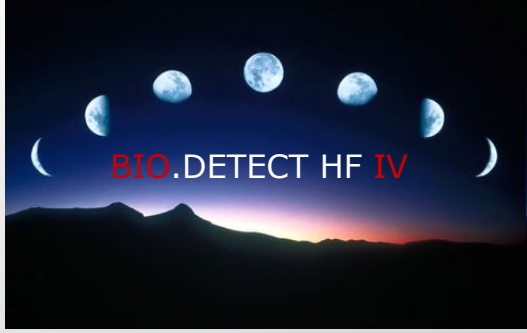
- **subjects who have already received and ICD and/ or CRT-D therapy within 12 months before study participation.**
- **LVEF ≤ 35%;**
- **NYHA Class II or III Heart Failure;**
- **Men and women 18 years of age or older;**
- **Understand the nature of the procedure;**
- **Give written informed consent**

Exclusion Criteria

Main Exclusion Criteria

- No indication or contraindication for ICD or CRT-D therapy;
- Permanent AF;
- NYHA Class IV Heart Failure;
- Subjects with irreversible brain damage from preexisting cerebral disease;
- Subjects with acutely decompensated heart failure;
- Expected heart transplantation within next six months or planned cardiac surgery within next 3 months, or life expectancy less than six months.
- Unstable geographical residence and/or GSM-free residence;

Sample size and study duration



- Event-driven Study, collecting 50 primary endpoint events.
- 625 subjects to enroll, including dropouts
- enrollment period: of 3 years
-
- overall study duration: 4 years (expected mean follow-up period: 1 year).

Non-invasive Monitoring systems

	Recommended assessment frequency*	Methods of measurement
Non-invasive variables		
Systolic and diastolic blood pressure (mm Hg)	Daily	By the patient (via device)
Pulse rate (beats per min)	Daily	By the patient (via device)
3-lead ECG	Daily	By the patient (via device), electrode placement needed
Systolic time intervals	Daily	By the patient (via ECG)
Heart rate variability	Daily	By the patient (via ECG)
Bodyweight (kg)	Daily	By the patient (via device)
Blood glucose	Individually	By the patient (via device with blood sample)
Plasma concentrations of natriuretic peptides	Weekly–monthly	By the patient (via device with blood sample)
Oxygen saturation	In case of emergency	By the patient (via device)
Variables derived by acoustic cardiography	Daily	By the patient (via device)
Self-administered questions	Daily–monthly	By the patient (device-administered questionnaire [ie, device asks the questions])

Anker SD, Koehler F, Abraham WT. Telemedicine and remote management of patients with heart failure. Lancet 2011; 378: 731–39

Invasive Monitoring

Pulmonary Artery Pressure Monitoring system: CardioMEMS sensor and transmitter

- **Implantable haemodynamic monitors that can remotely monitor changes in intra cardiac or pulmonary artery pressures**

Abraham WT et al. *Lancet*, 2011; 377: 658-666_CHAMPION Trial