Telemonitoring in heart failure: IN TIME and beyond

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Presenter Disclosure Information

Gerhard Hindricks has received honoraria for lectures from Biosense, Stereotaxis, St. Jude Medical, Biotronik

Gerhard Hindricks is a member of the Adivisory Board / consultant for Biosense, St. Jude Medical, Biotronik,,

Telemedicine and heart failure: Expectations

- Guide heart failure therapy
- Early detection of HF worsening
- Prevention of HF decompensation
- Reduction of mortality, especially HF mortality
- Reduction of hospitalizations, especially HF hospitalizations
- Improvement of QoL
- Reduction of treatment costs

Telemonitoring and heart failure: Tele HF-Study

- 1653 pts. (61 yrs, 50% CAD, 50% NYHA III) with recent HF hospitalization were randomized to telemonitoring or conventional treatment

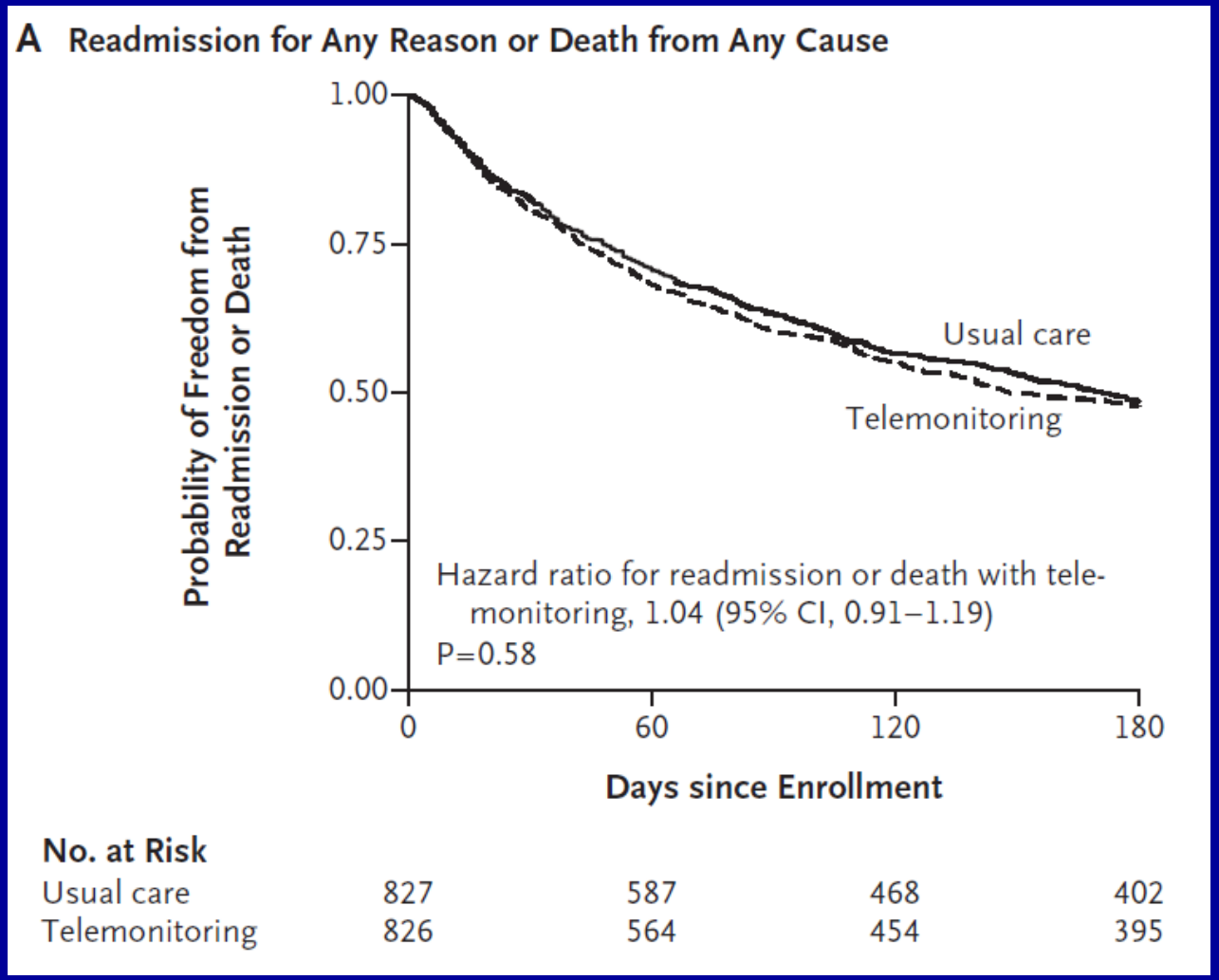
- Interactive automatic voice response system
  - weight and clinical symptoms

  Primary outcome parameter was mortality and any re-hospitalization

- Secondary outcome parameters: heart failure re-hospitalization, days in hospital, no. of hospitalizations

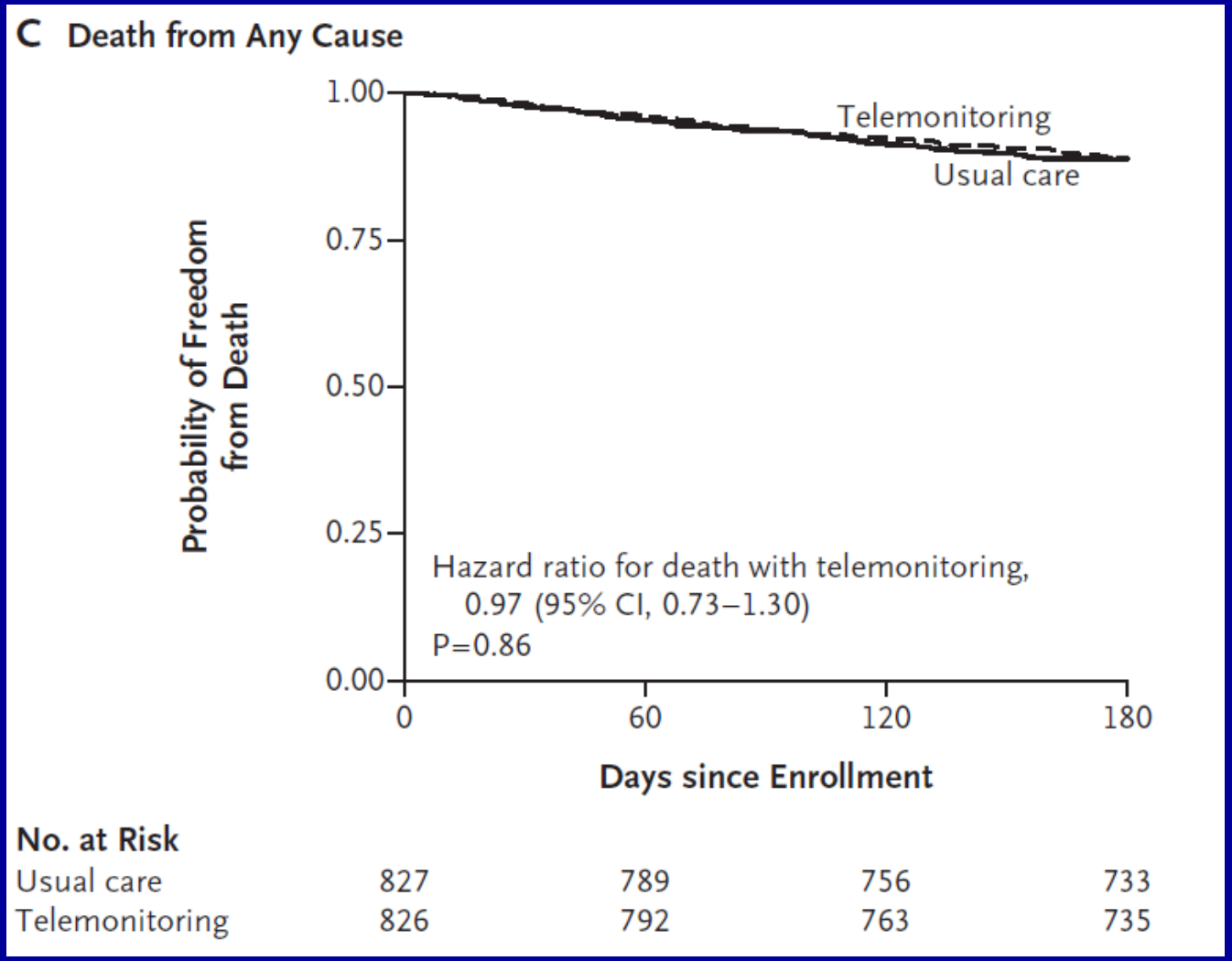
Chaudhry SI et al., NEJM 2011

Telemonitoring and heart failure: Tele HF-Study



Chaudhry SI et al., NEJM 2011

Telemonitoring and heart failure: Tele HF-Study



Chaudhry SI et al., NEJM 2011

Telemonitoring and heart failure: Tele HF-Study

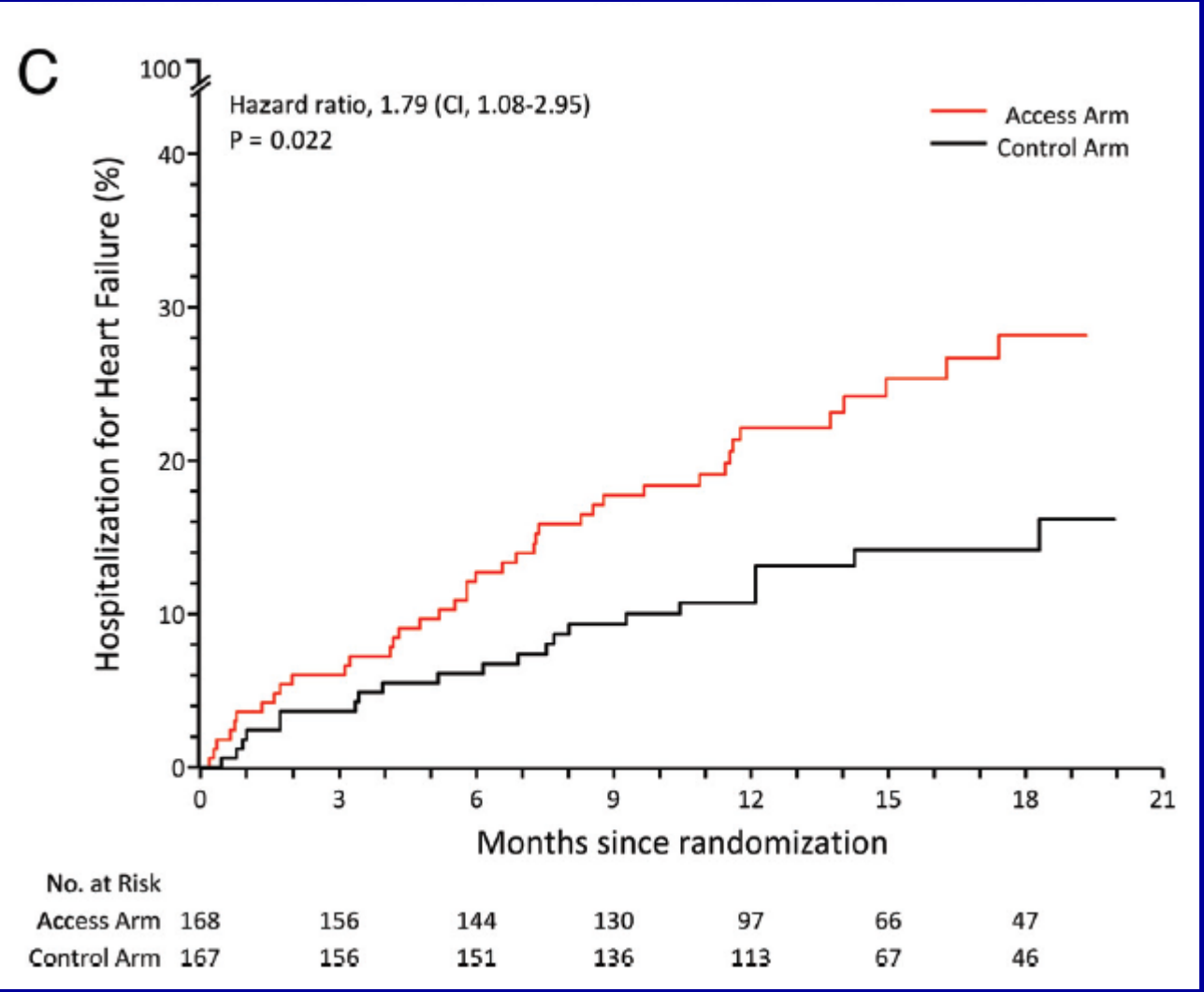
- Potential explanations for negative study outcome:
  - not the right patients selected/included
  - not the optimal monitoring parameter
  - not the optimal mode of monitoring
  - patient compliance and time windows
- Telemonitoring simply does not improve HF therapy

Automatic impedance alert: Dot HF- Study

- Prospective randomized evaluation of thoracic impedance based automatic patient alert to improve outcome in NYHA III ICD/CRT patients
- Primary endpoint was heart failure hospitalization and all cause mortality
- 335 pts. included [18% ICD, 82% CRT]
- Alert in case of preset impedance threshold crossing
- Follow up was 14.9 months

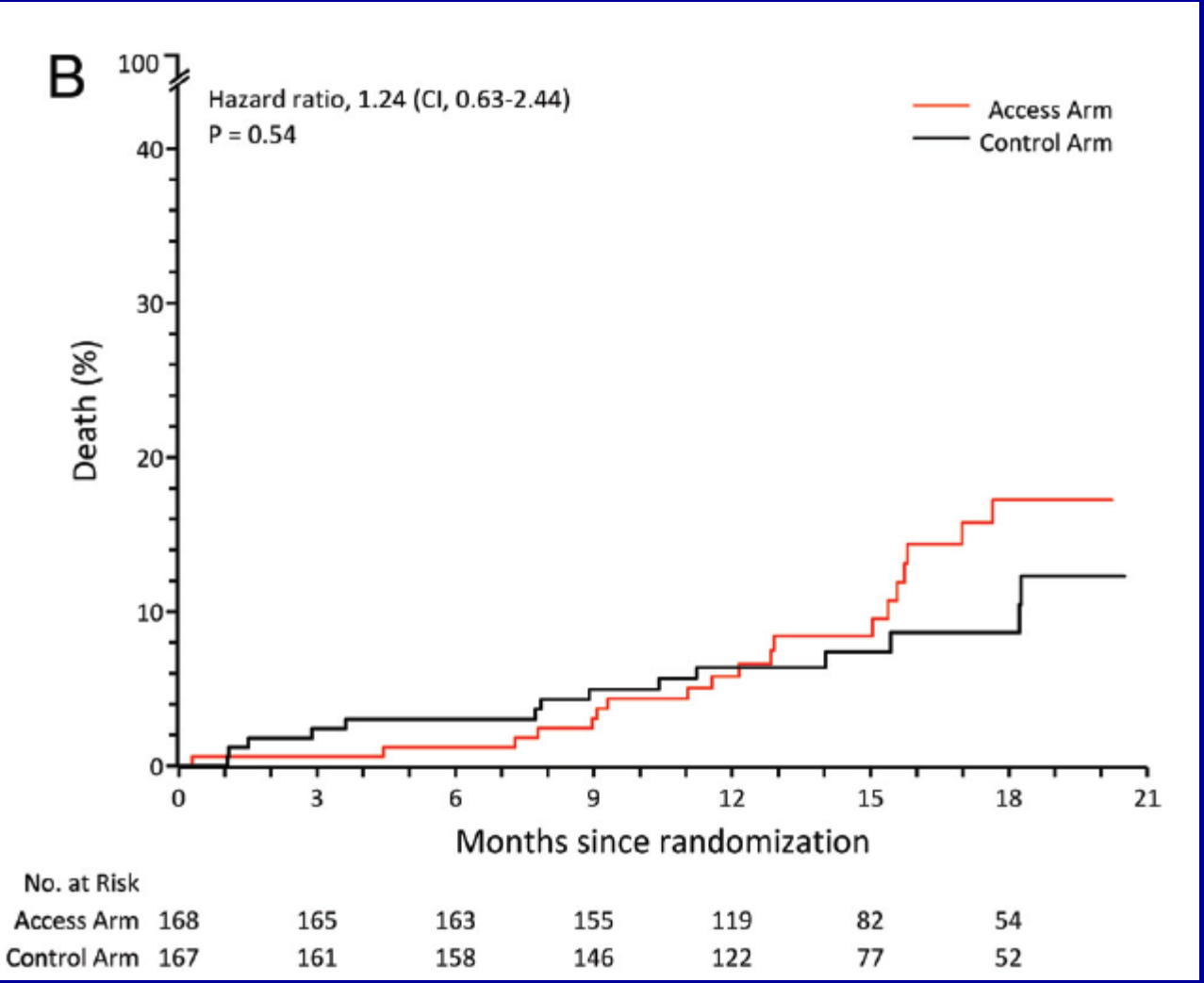
van Veldhuisen et al., Circulation 2011

Dot HF- Study: Hospitalization for heat failure



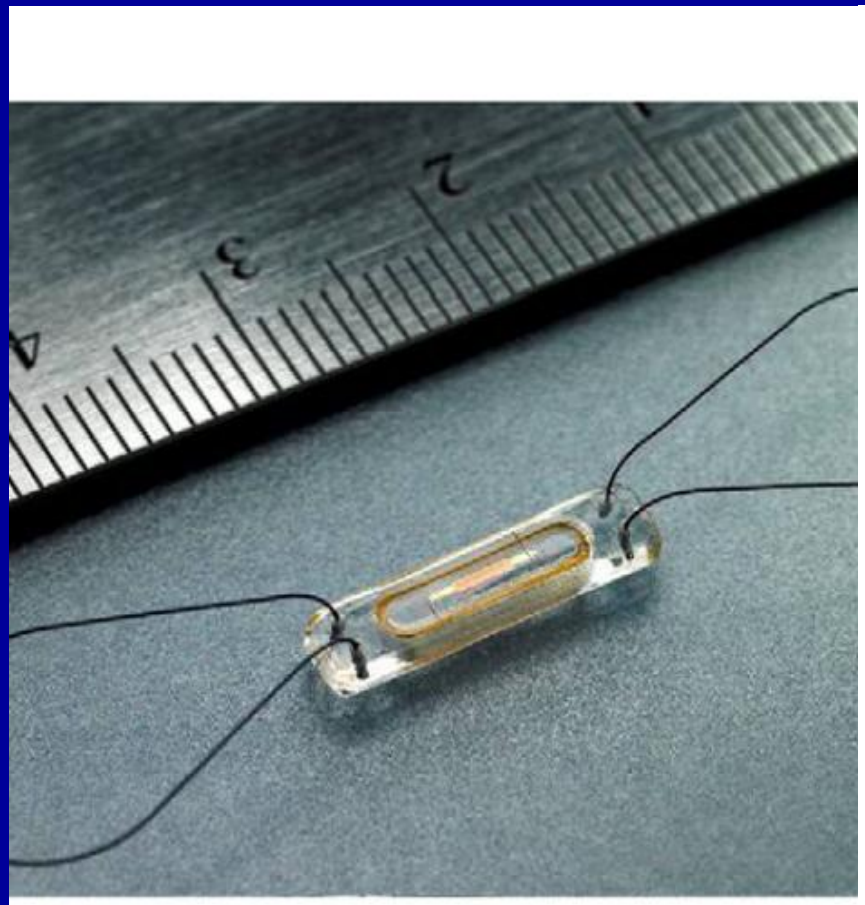
van Veldhuisen et al., Circulation 2011

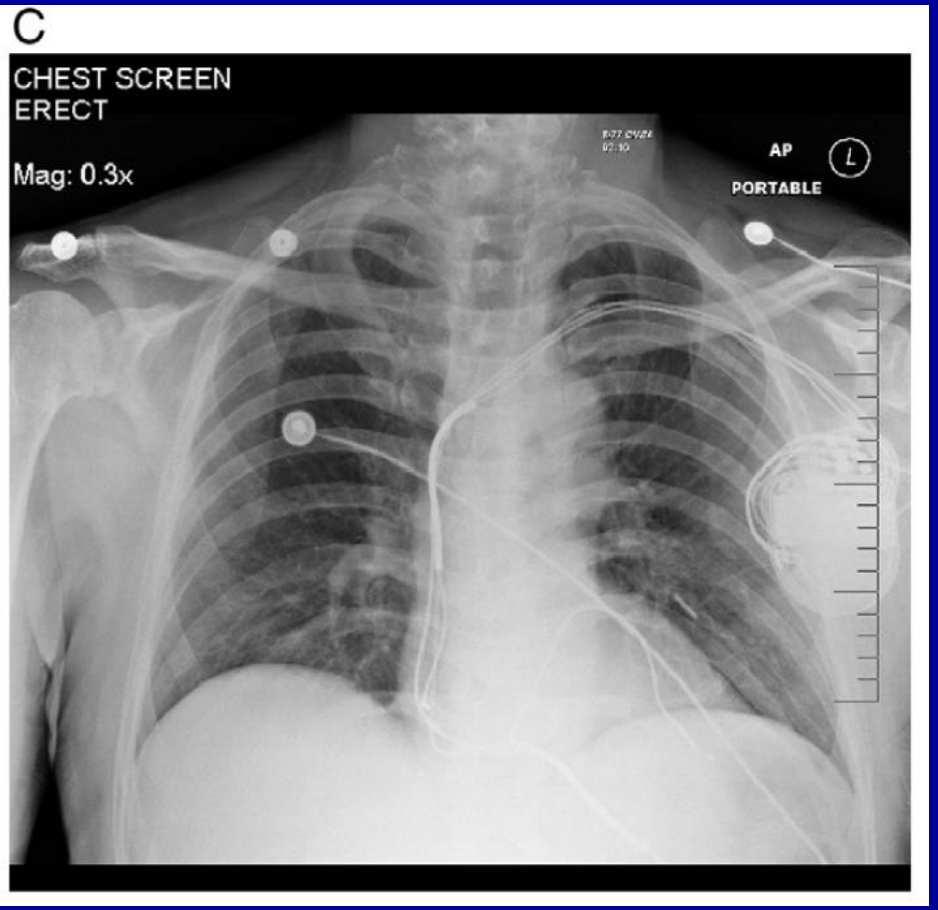
Dot HF- Study: all cause mortality



van Veldhuisen et al., Circulation 2011

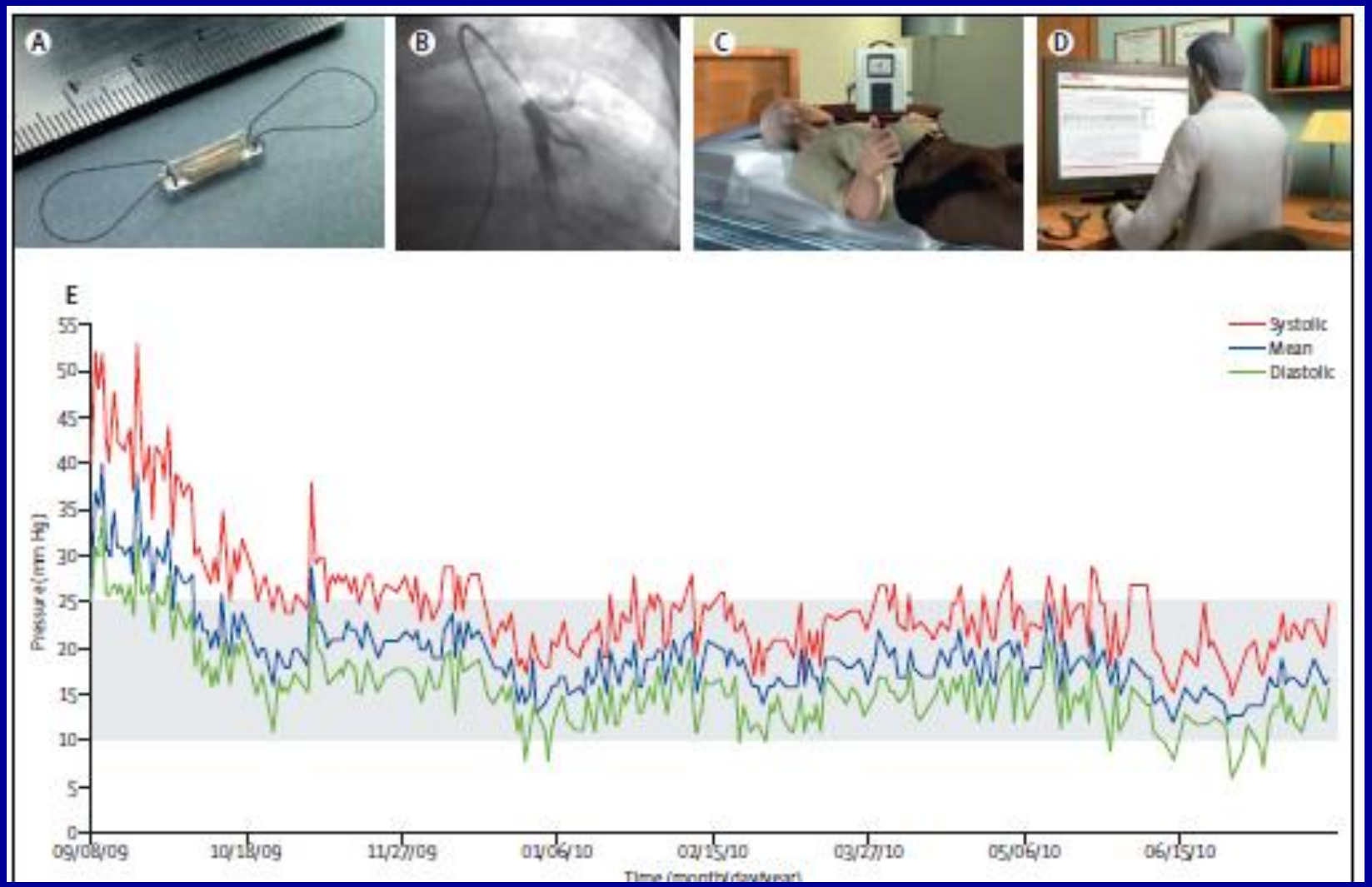
Pulmonary artery pressure monitoring: Champion Trial





Abraham WT et al., Am Heart J 2011

Pulmonary artery pressure monitoring: Champion Trial



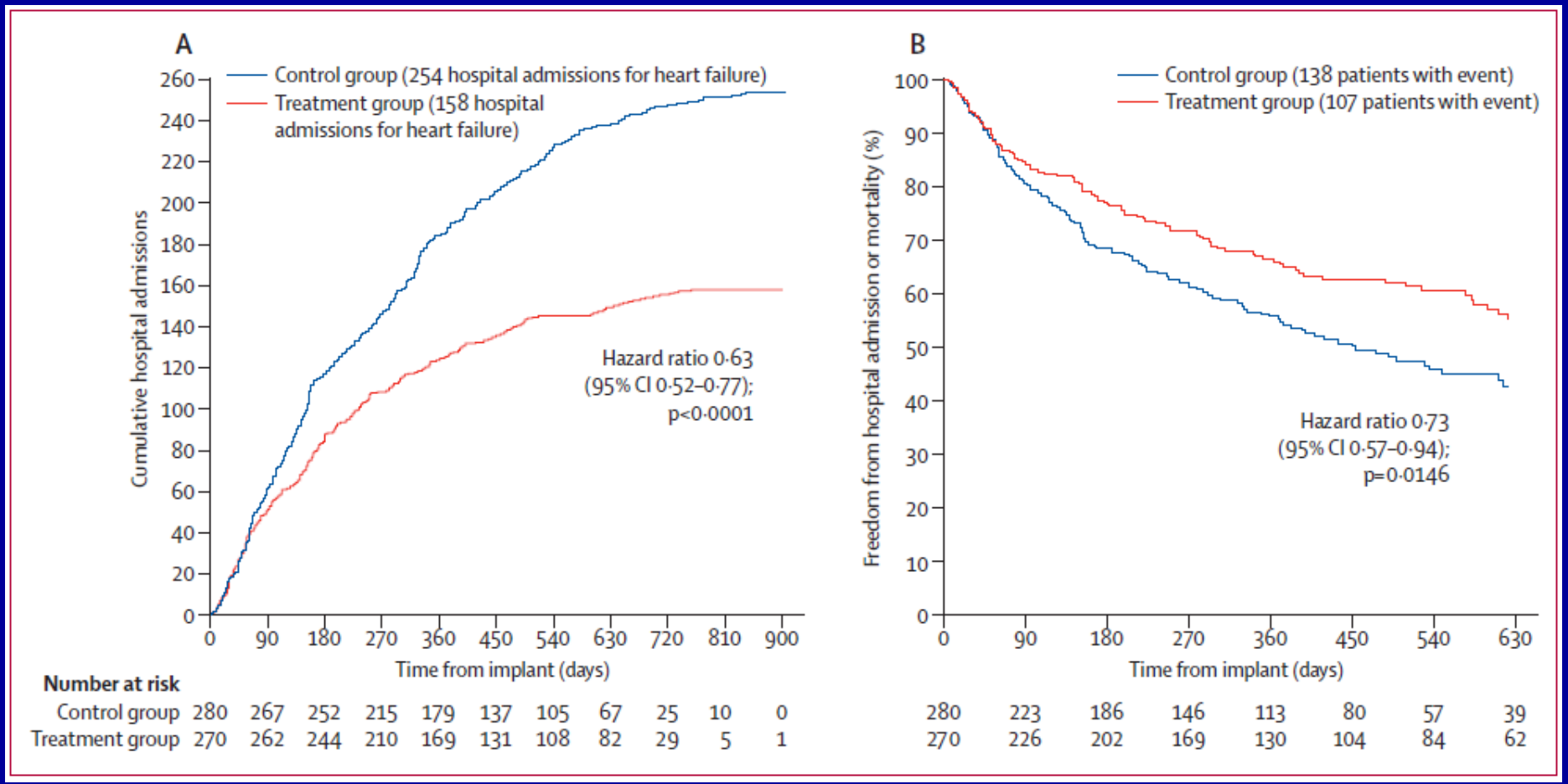
Abraham WT et al., Lancet 2011

Pulmonary artery pressure monitoring: Champion Trail

- Wireless implantable hemodynamic monitor (W-IHM) was placed percutaneously in 550 pts. with advanced heart failure
- Single blinded design; primary endpoint was heart failure related hospitalizations
- 83 HF hospitalizations occurred in 270 “on” pts.
- 120 HF hospitalization occurred in 280 “off” pts.
- Use of W-IHM data reduced HF hospitalizations by 39%

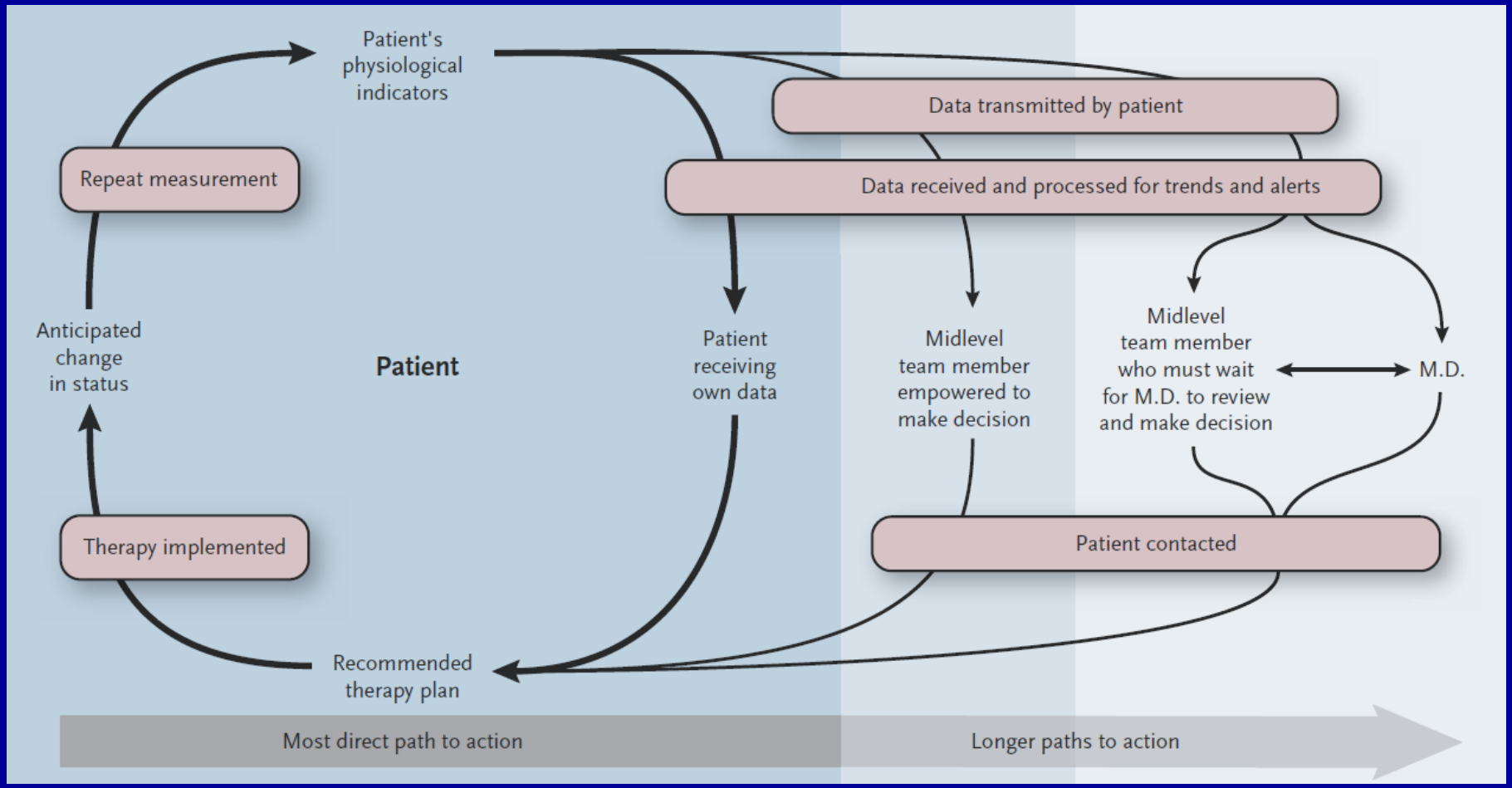
Abraham WT et al., Lancet 2011

Pulmonary artery pressure monitoring: Champion Trial



Abraham WT et al., Lancet 2011

Home monitoring and heart failure: Background



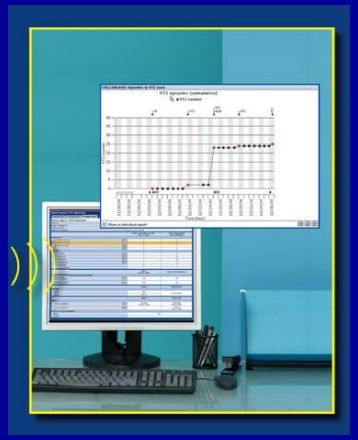
Desai AS and Stevenson LW; NEJM 2010

Advanced Home Monitoring
Operating Principles

A highly reliable RF transmitter integrated into the ICDdevice sends patient and device data on command

The Cardio Messenger relays data to the Service Center using integrated cellular, and/or standard telephone technology for unsurpassed mobility and coverage.

Data is stored and formatted into a Cardio Report with informative trends, charts, parameters, IEGMs and graphs.



Critical patient and device data is transmitted immediately to the physician via Internet, E-mail, pager, cell phone, or fax.
Trend analysis and status reporting are delivered on a periodic basis.

Home monitoring and heart failure: concept

- Automatic acquisition and transmission of data during follow-up
- No direct patient involvement
- Immediate access to data
- Short intervention times
- Automatic control / assessment of intervention result

- Which data are predictive for heart failure outcome?

Home monitoring and heart failure: Home Care Study

- Retrospective evaluation of parameters indicative for heart failure decompensation and death
- 377 patients with advanced heart failure were followed for 12 months after HM CRT device implantation
- Pre-defined parameters were assess in the time window of 25 – 3 days before hospitalization or death
- Sensitivity and specificity for prediction of (I) hospitalization and (II) death were calculated

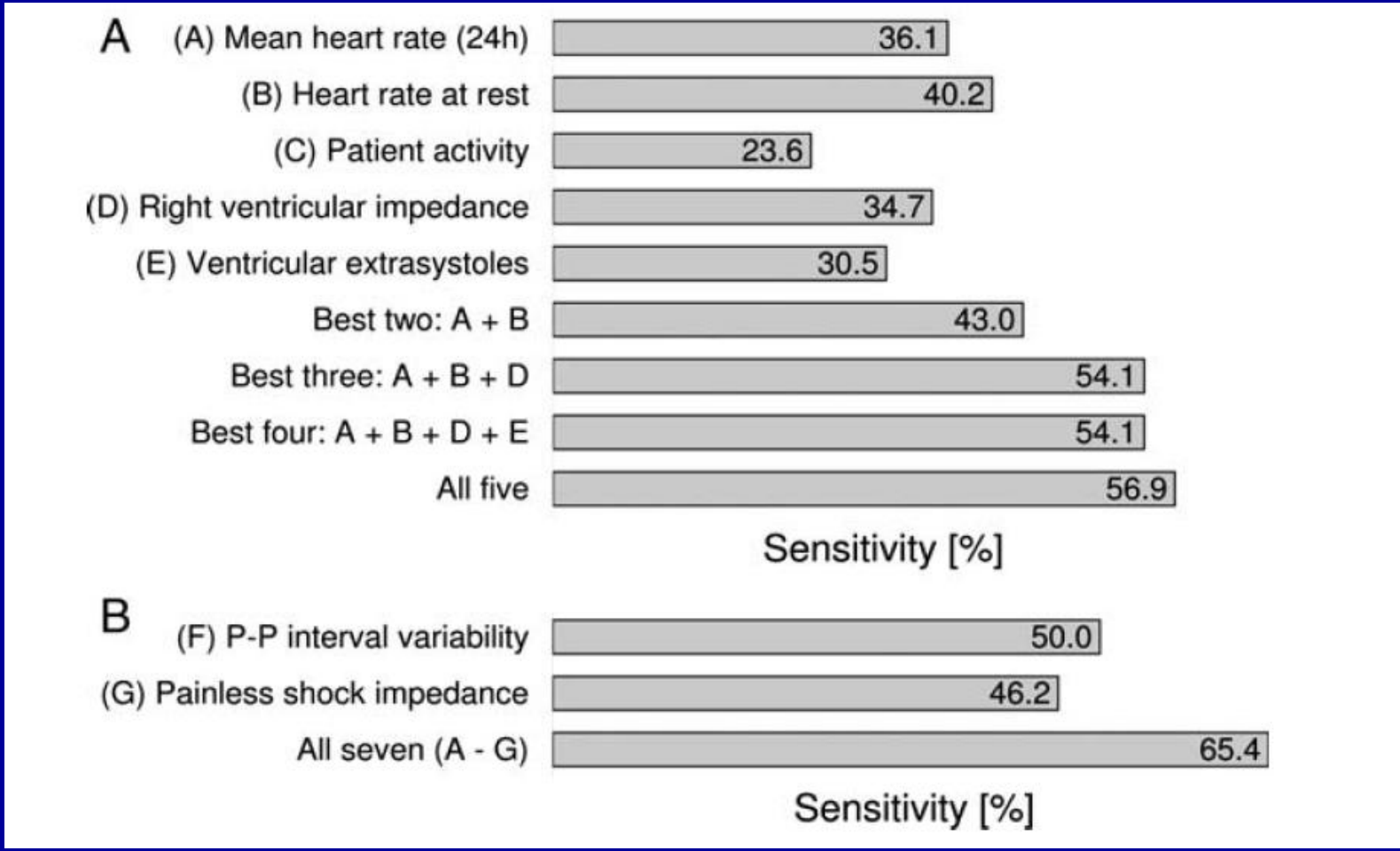
Sack S et al., Eur J Heart Fail 2011

Home monitoring and heart failure: Home Care Study

Parameter	*n* = 377
Age (years), mean (SD)	66.2 (10.0)
Female, %	21.5
LVEF (%), mean (SD)	24.5 (7.5)
% of patients with LVEF ≤35%	90.7
LVEDD (mm), mean (SD)	67.8 (15.8)
Aetiology of heart failure, %	
Ischaemic (of which, myocardial infarction)	55.7 (75.2)
Non-ischaemic	44.3
NYHA class, %	
I	0.8
II	14.9
III	74.8
IV	8.5

Sack S et al., Eur J Heart Fail 2011

Home Care: sensitivity to detect major CV event



Sack S et al., Eur J Heart Fail 2011

Home Care Study: results

- Retrospective sensitivities for individual parameters ranged from 23.6 – 50%.
- Optimal combination of parameters increased sensitivity to 65.4% for cardiovascular hospitalization and death with a 99.5% specificity
- This corresponds to 1.83 false-positive detections per patient-year of follow-up
- These results need to be confirmed in prospective studies

Sack S et al., Eur J Heart Fail 2011

The In Time Trial

- Prospective, randomized, controlled, international
- 720 HF patients, 50 centers

- Inclusion criteria:
  - ICD indications (dual chamber ICD, CRT-D)
  - Chronic heart failure (≥ 3 months)
  - NYHA Class II or III for 1 month prior to screening
  - LVEF ≤ 35% within 3 months prior to screening
  - Indication for therapy with diuretics

Hindricks et al.; Lancet 2014, in press

Primary end point: Packer Score

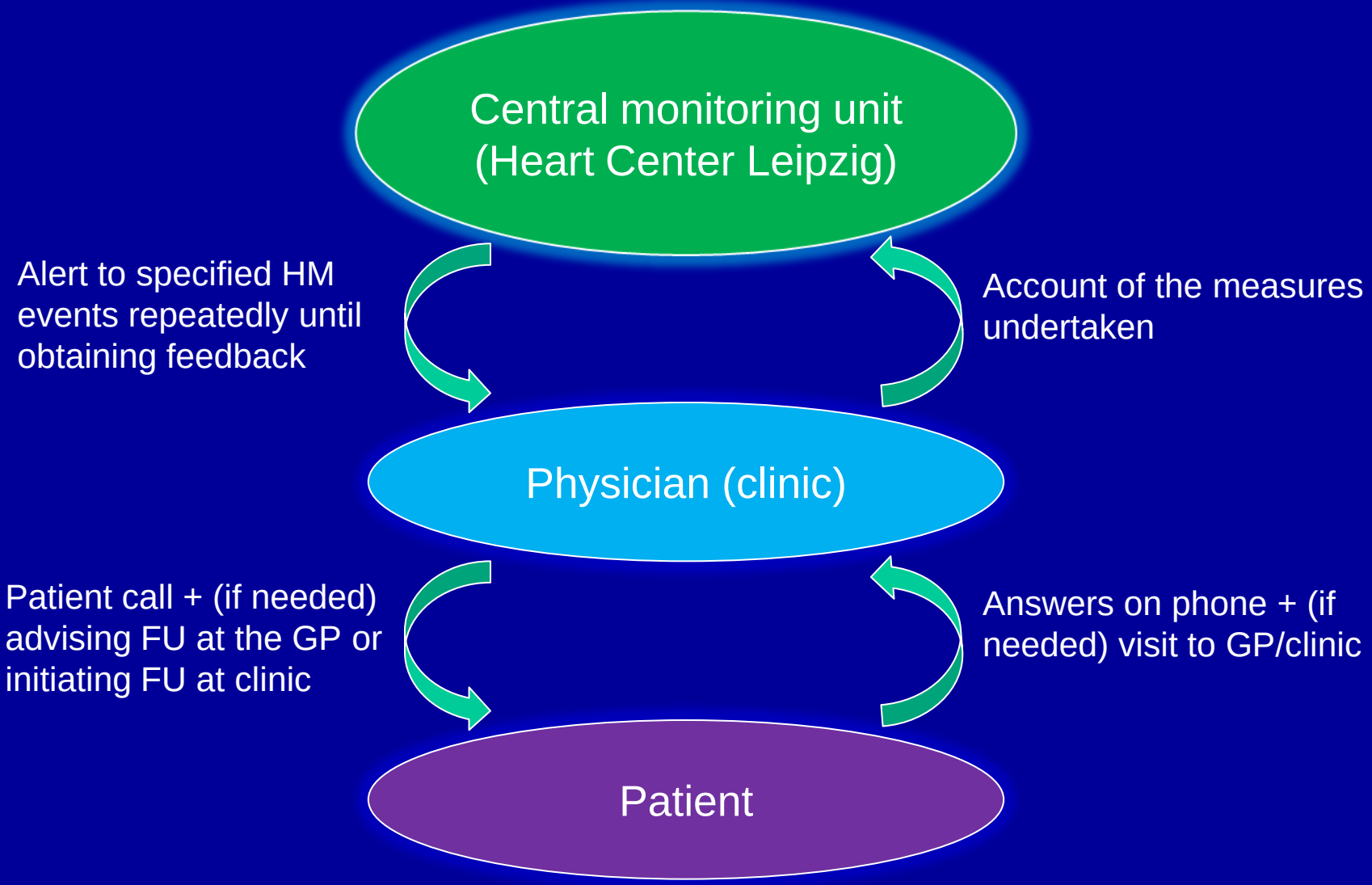
- Each patient is classified by the end of the study as:
  - Improved
  - Unchanged
  - Worse
- Based on events such as:
  - Death
  - Overnight hospitalization for worsening heart failure
  - Favorable, unfavorable or no change in NYHA class
  - Improvement, deterioration or no change in the patient's global assessment score
  - Discontinuation of study protocol due to worsening heart failure, treatment failure or lacking therapeutic response

Packer J Card Fail 2001;7:176-82

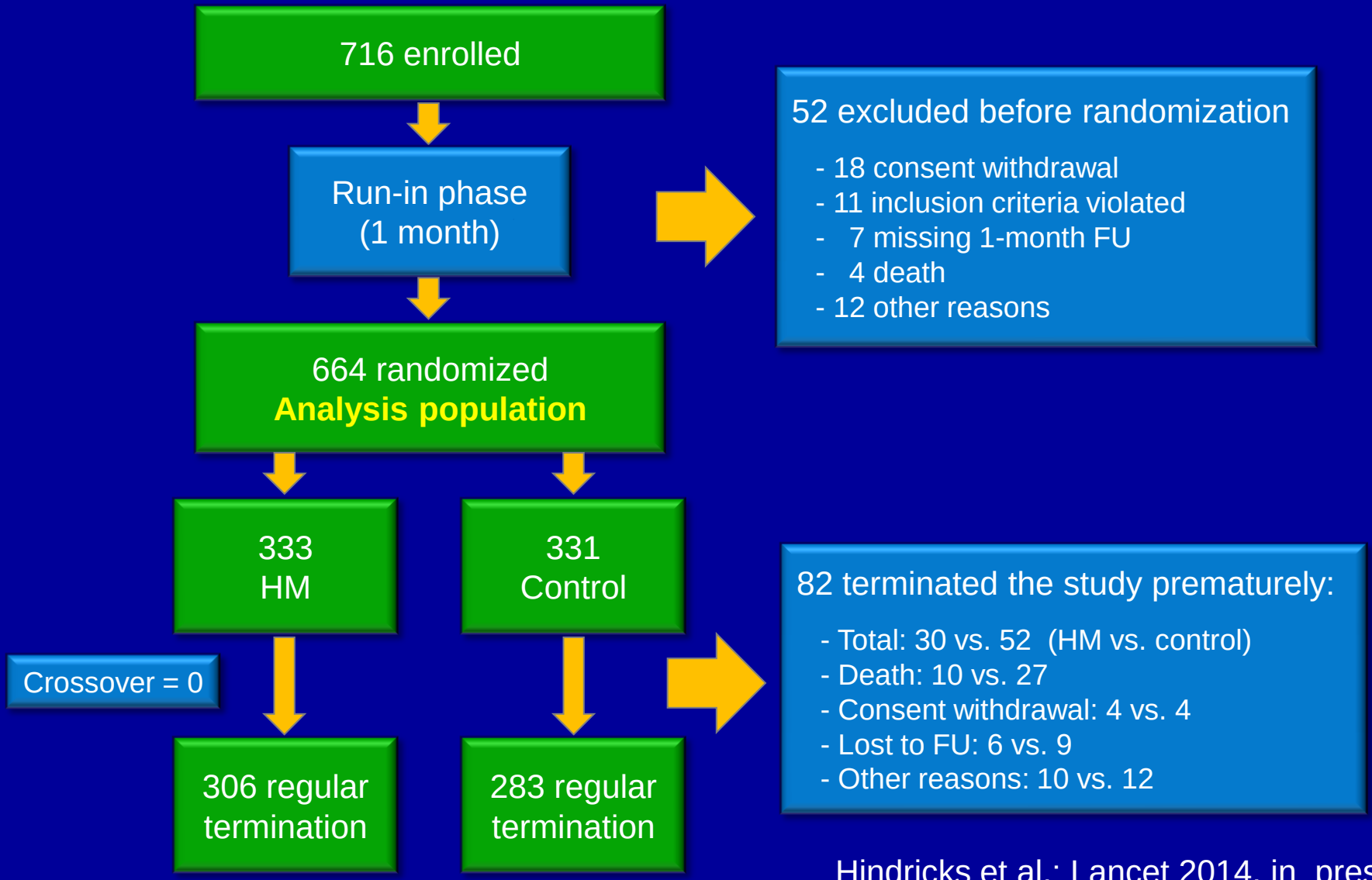
The In Time Study: Secondary end points

- All-cause mortality
- Number of re-hospitalizations (> 1 day) due to worsening heart failure
- Correlation of values of HM parameters with the clinical status
- Incidence and reasons for HM based interventions
- Additional follow ups due to technical HM messages
- HM workflow analysis

Centralized Home Monitoring organization



In Time: Patient flow



Hindricks et al.; Lancet 2014, in press

In Time: Demographics and medical history of analysis population at enrollment

	All	HM	Control
Total Recruitment	664 (100)	333 (50,2)	331 (49,8)
Age, years	65,5 ± 9,4	65,3 ± 9,3	65,8 ± 9,6
Female	129 (19,4)	60 (18)	69 (20,8)
Aetiology			
Ischemic	458 (69)	233 (70)	225 (68)
Non-ischemic	206 (31)	100 (30)	106 (32)
Cardiovascular and pulmonary medical history			
Hypertension	463 (69,7)	242 (72,7)	221 (66,8)
Stroke/TIA	72 (10,8)	40 (12,0)	32 (9,7)
Chronic obstructive pulmonary disease	94 (14,2)	48 (14,4)	46 (13,9)
Atrial Fibrillation	168 (25,3)	76 (22,8)	92 (27,9)
Diabetes	266 (40,1)	131 (39,3)	135 (40,8)
Renal insufficiency	199 (30)	99 (29,7)	100 (30,2)

Mean ± SD, or n (%)

Hindricks G et al., Lancet 2014, in press

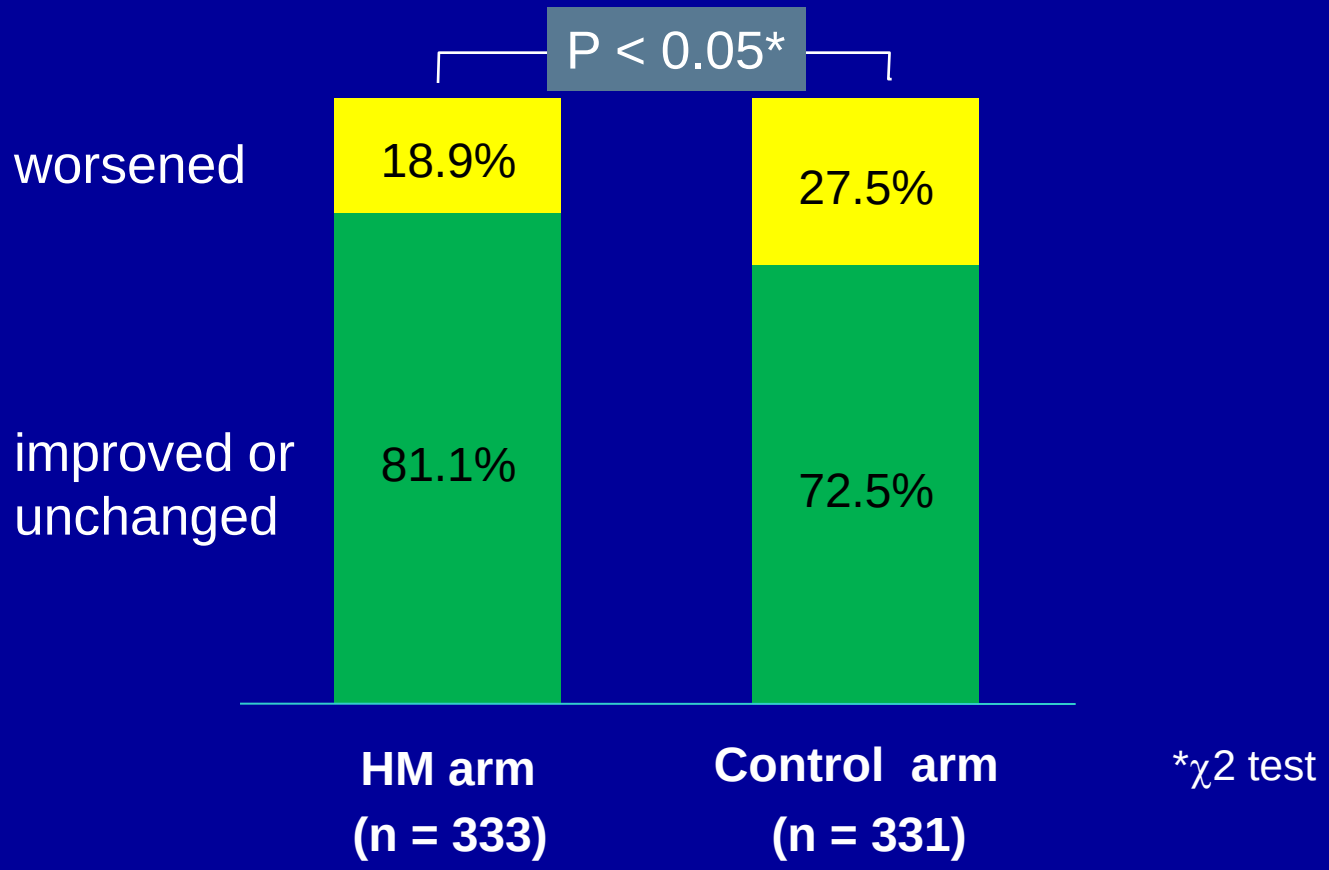
Status at enrollment

	All	HM	Control
Height (cm)	172 ± 9	173 ± 9	172 ± 9
Weight (kg)	84 ± 16	84 ± 16	83 ± 16
BMI	28 ± 4,6	28 ± 4,4	28,1 ± 4,7
NYHA			
Class II	285 (43)	150 (45,2)	135 (40,8)
Class III	378 (57)	182 (54,8)	196 (59,2)
LVEF, %	25,8 ± 6,6	26 ± 6,5	25,6 ± 6,6
Intrinsic QRS duration, ms	134 ± 34	135 ± 33	133 ± 36
Resting heart rate	70,2 ± 13,8	70,3 ± 13,8	70,1 ± 13,9
Indication for defibrillator			
Primary prophylaxis	525 (79,1)	265 (79,6)	260 (78,5)
Secondary prophylaxis	139 (20,9)	68 (20,4)	71 (21,5)
SCA with documented VT/VF	31 (4,7)	13 (3,9)	18 (5,4)
SCA with inducible VT/VF	26 (3,9)	15 (4,5)	11 (3,3)
Implanted device			
CRT-D	390 (58,7)	190 (57,1)	200 (60,4)
ICD	274 (41,3)	143 (42,9)	131 (39,6)

Mean ± SD, or n (%)

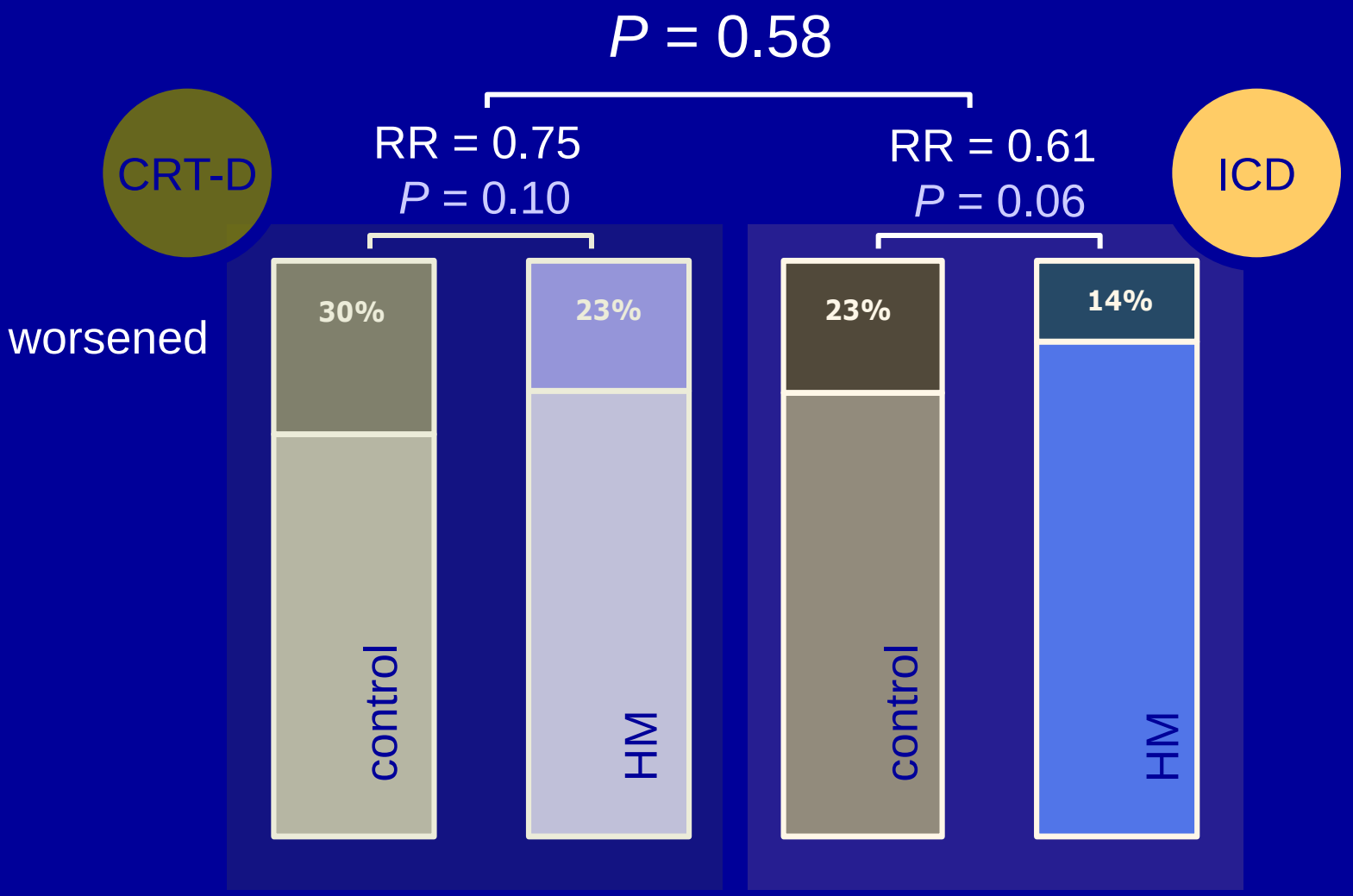
Hindricks G et al., Lancet 2014, in press

In Time Results: modified Packer Score

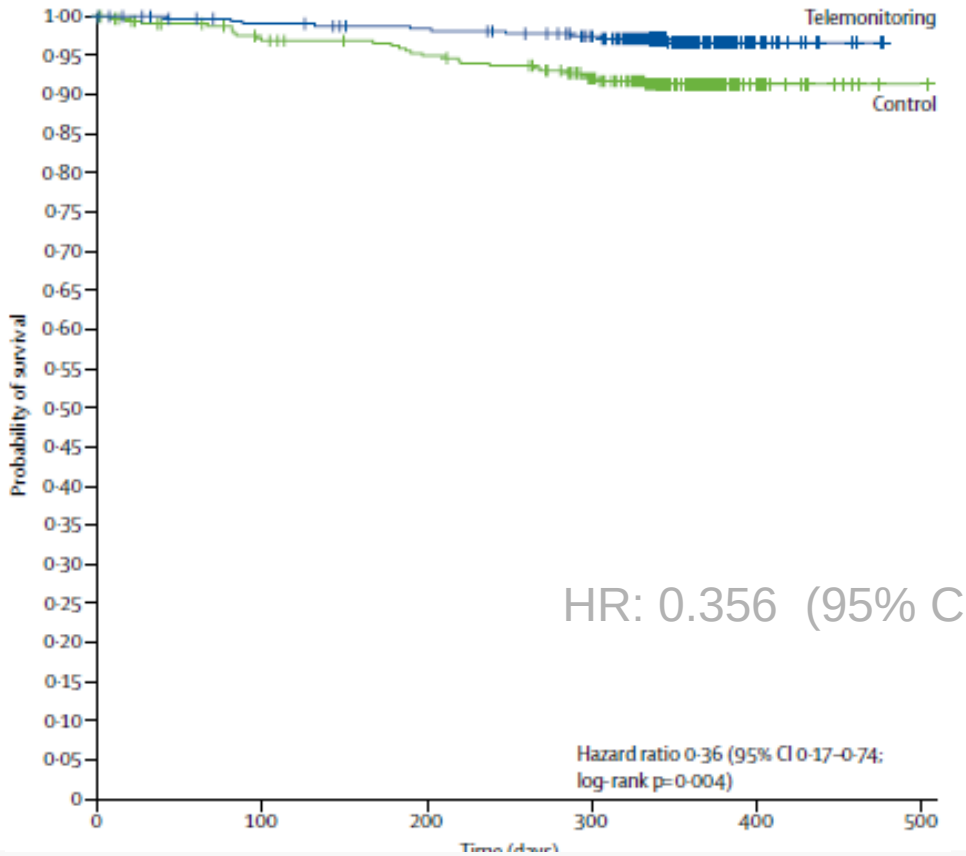


Hindricks G et al., Lancet 2014, in press

In Time Results: CRT D versus ICD



All-cause mortality

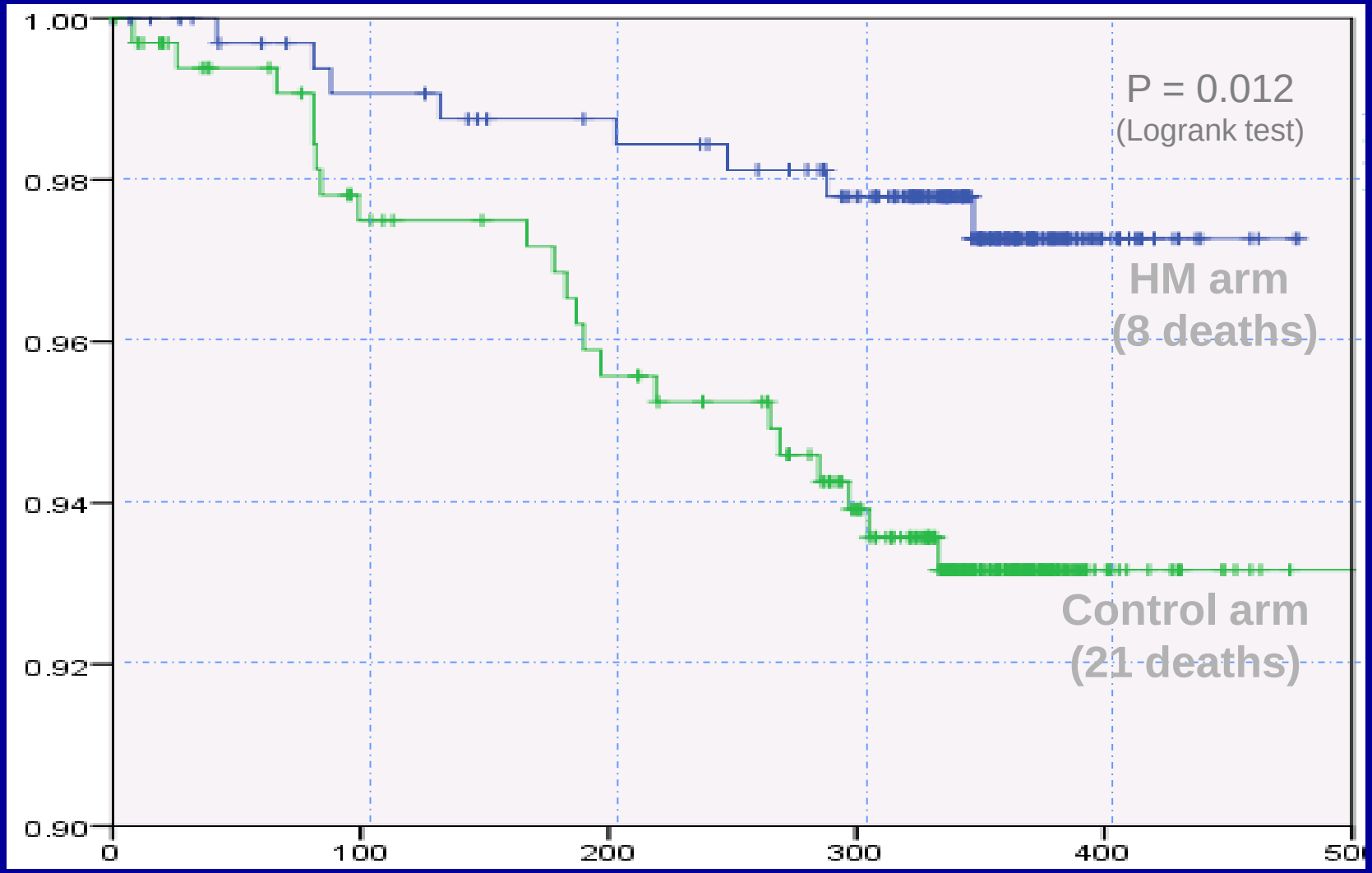


HR: 0.356 (95% CI: 0.172–0.735)

Hindricks et al.; Lancet 2014

Cardiovascular mortality

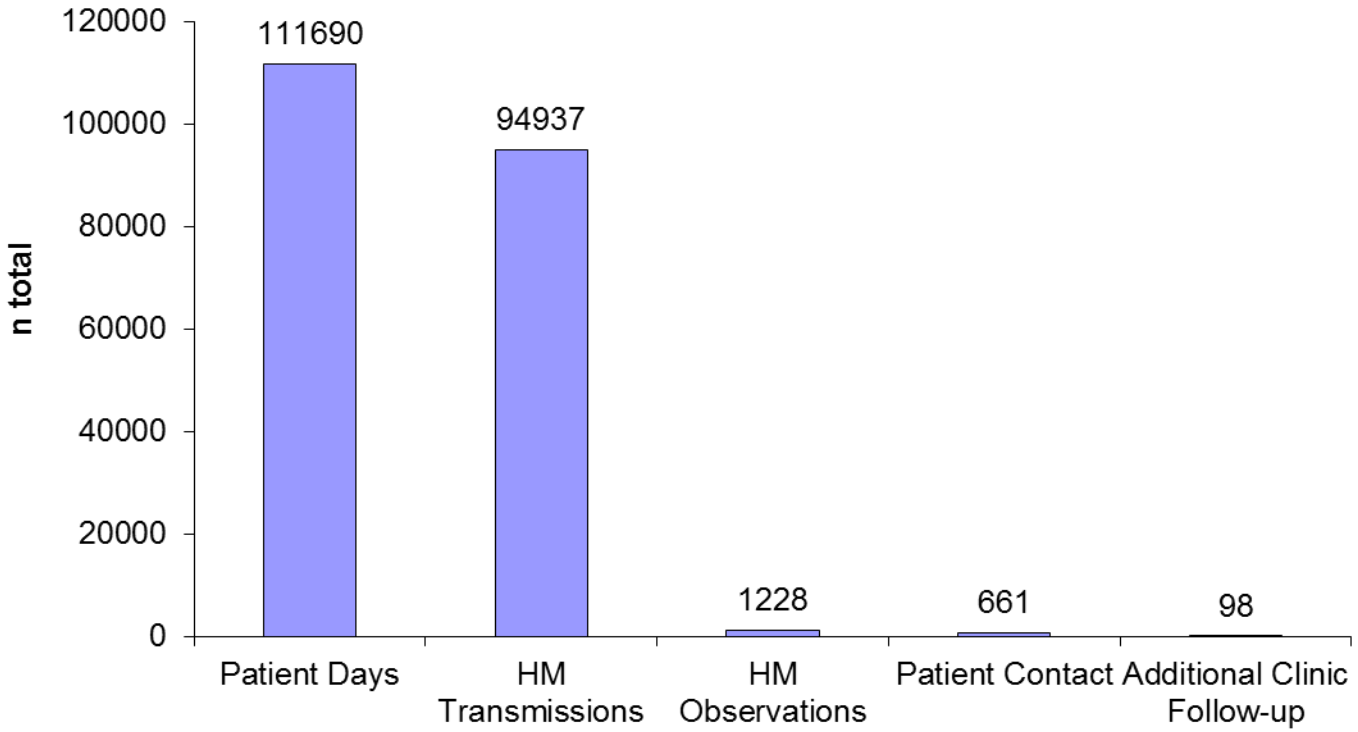
HR: 0.367 (95% CI: 0.162–0.828)



Transmission reliability and related workload

Transmissions received: > 85 %

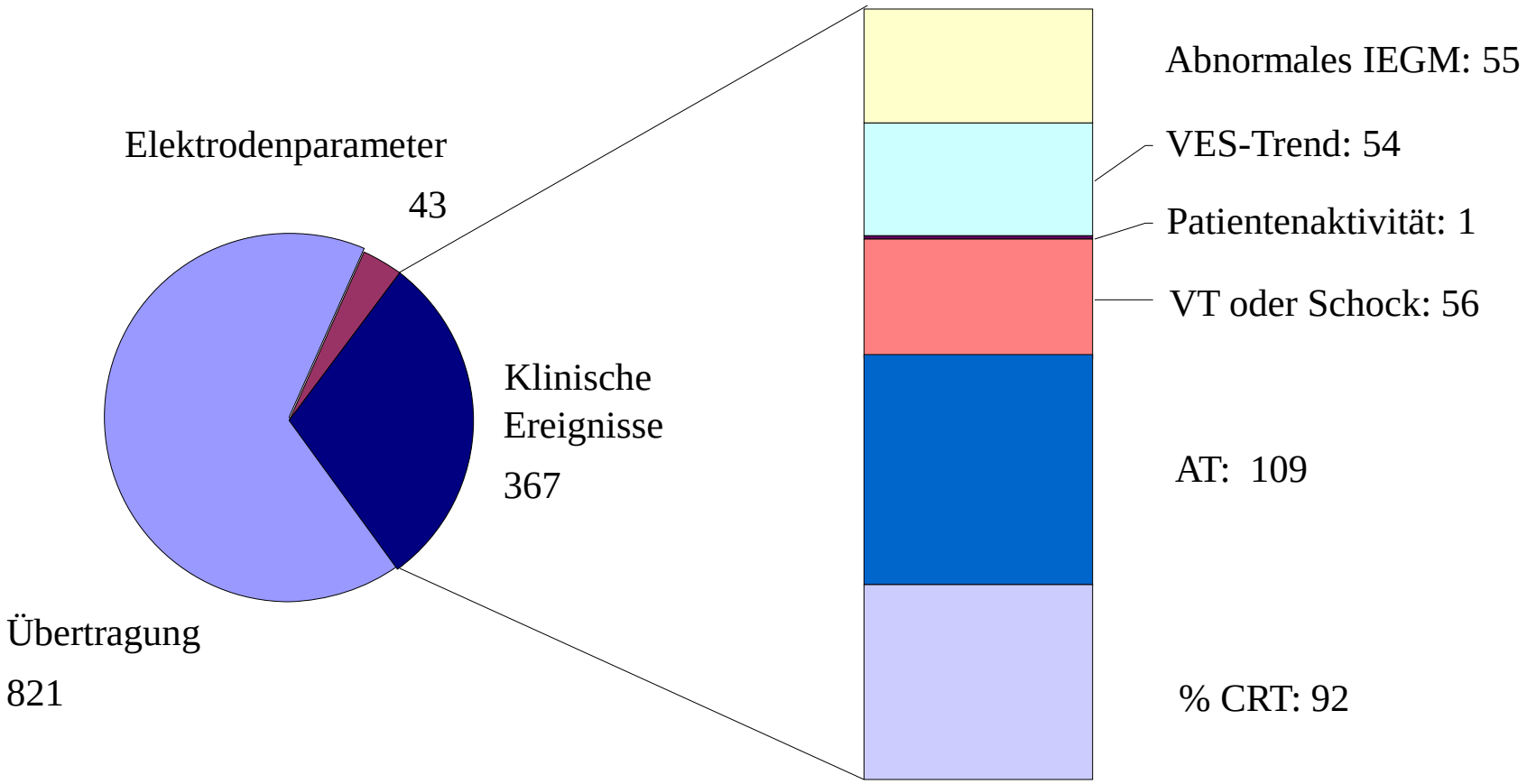
additional workload: 0,3 in-hospital visits per patient year



85 % **4 /Jahr** **2,2 /Jahr** **0,3 /Jahr**

306 patient years

Main events triggering further care



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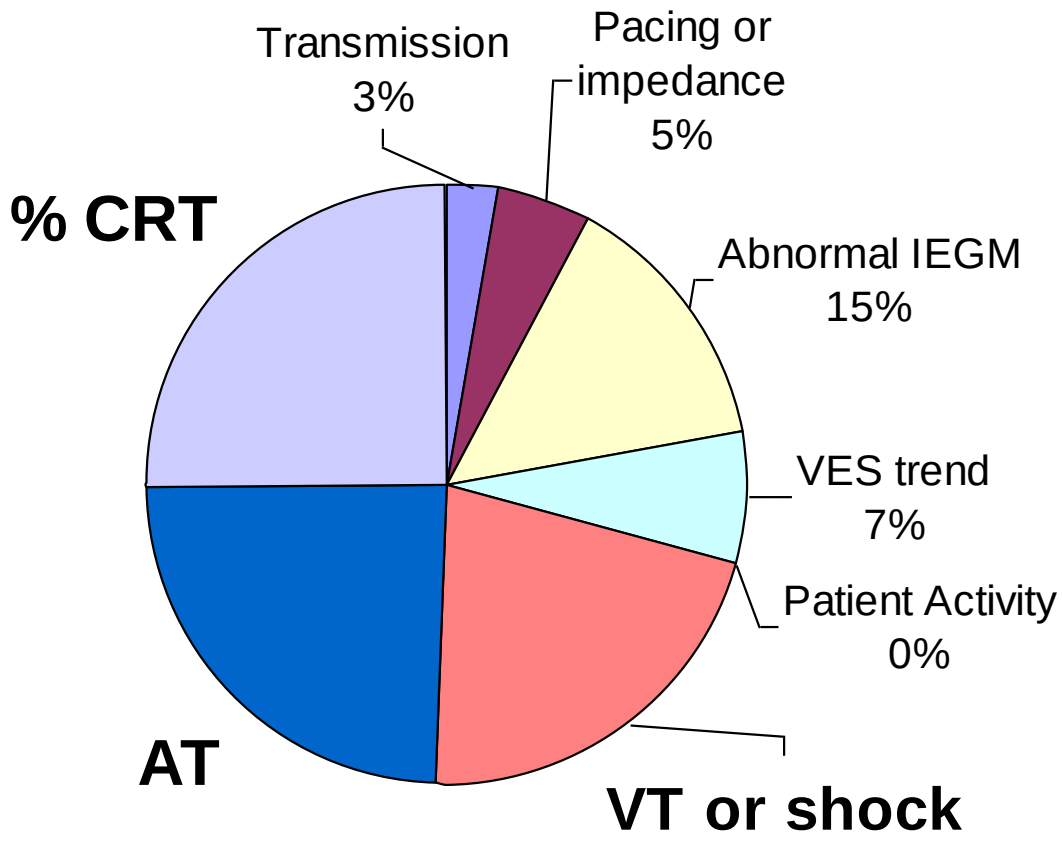

Conclusions

- 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.

In-Time investigational sites (36):

Australia (1):
Wahroonga (Sydney Adventist Hospital)

Austria (1):
Innsbruck (Uni-klinik für Innere Medizin)

Czech Republic (2):
Prague (IKEM)
Prague (Na Homolce)

Denmark (3):
Aalborg (Aalborg Hospital)
Aarhus (Uni-hospital, Skejby Sygehus)
Hellerup (Gentofte Hospital)

Germany (26):
Bad Berka (Zentralklinik Bad Berka)
Bad Neustadt (Herz- und Gefäß-Klinik)
Bad Segeberg (Segeberger Kliniken)
Berlin (Charité – Campus Benjamin Franklin)
Berlin (Vivantes Humboldt-Klinikum)
Berlin (Vivantes Klinikum am Urban)
Berlin (Vivantes Klinikum Neukölln)
Bielefeld (Städtische Kliniken Bielefeld Mitte)
Bonn (Uni-klinikum Bonn)

Germany continued:
Coburg (Klinikum Coburg)
Detmold (Klinikum Lippe-Detmold)
Essen (Uni-klinikum Essen)
Hannover (MH Hannnover)
Homburg/Saar (Uni-klinikum des Saarlandes)
Leipzig (Herzzentrum Leipzig)
Leipzig (Klinikum St. Georg)
Lübeck (Uni-klinikum Schleswig-Holstein)
Lünen (St. Marienhospital Lünen)
München (Augustinum)
München (Herzzentrum München-Bogenhaus.)
München (Kard. Gem.-Praxis Dr. Mühling)
München (Klinikum Schwabing)
München (Klinikum Großhadern)
Nordhausen (Kard. Gemeinschaftspraxis)
Paderborn (St. Vincenz Krankenhaus)
Pirna (Klinikum Pirna)

Israel (2):
Ashkelon (Barzilai Medical Center)
Tel-Hashomer (Chaim Sheba Medical Center)

Latvia (1):
Riga (P. Stradins Clinical University Hosp.)