Pulmonary artery pressure management: importance of remote control in heart failure patients

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Cardiologia A-C Ciriè-Ivrea ASL TO4

Lo Scompenso Cardiaco è un onere clinico crescente

PREVALENZA

1-2%
Prevalenza[1]

15 M
pazienti con scompenso[2]

> 6 Milioni
nuovi casi di malattia cardiovascolare in UE ogni anno.[3]

INCIDENZA

1 su 5
persone svilupperà insufficienza cardiaca nel corso della sua vita.[4]

MORBILITA' E MORTALITA'

Pazienti AHA/ACC di grado C/D con diagnosi di scompenso cardiaco:

50%
Riammessi entro 6 mesi.[5]

50%
Tasso di mortalità combinato a 1 anno per scompenso cardiaco acuto e cronico.[6]

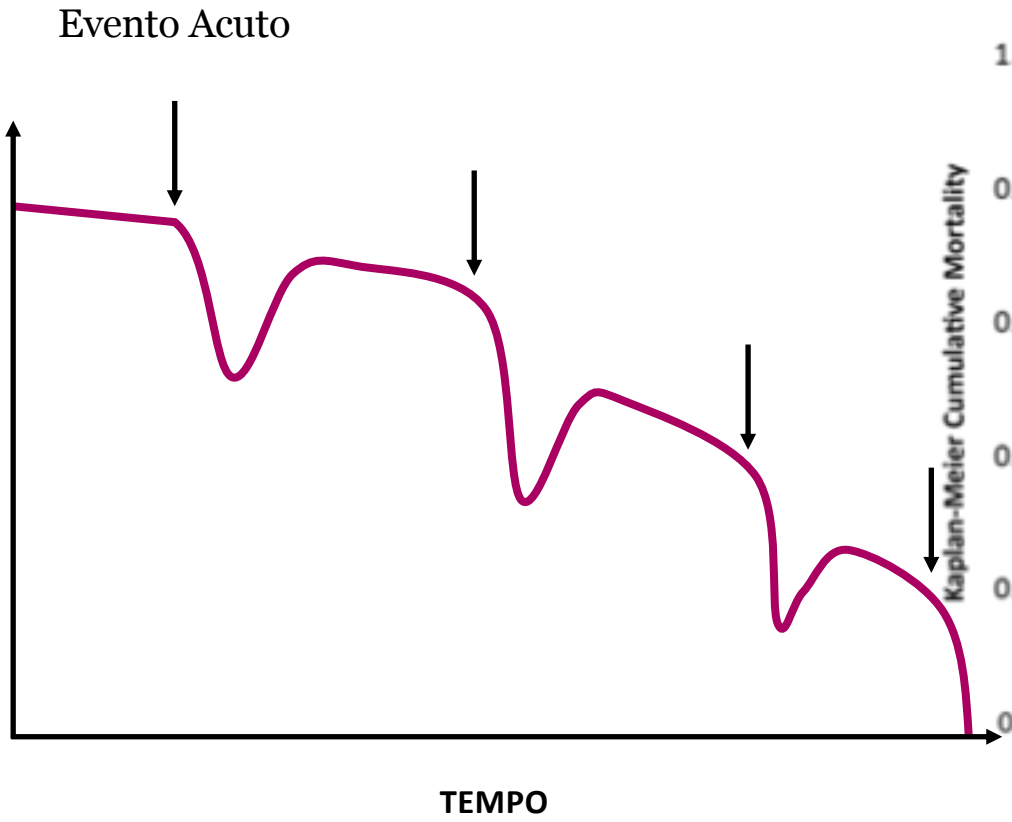
1. Cowie MR, et al. *Euro J Heart Failure*, 2017.
2. Ambrosy PA, et al. *J Am Coll Cardiol*, 2014.
3. Lloyd-Jones D, et al. *Circulation*, 2002.
4. ESC. European Heart Network, 2017.
5. Krumholz HM, et al. *Circ Cardiovas Qual Outcomes*, 2009.
6. Savarese G and Lund LH. Card Fail Rev, 2017.

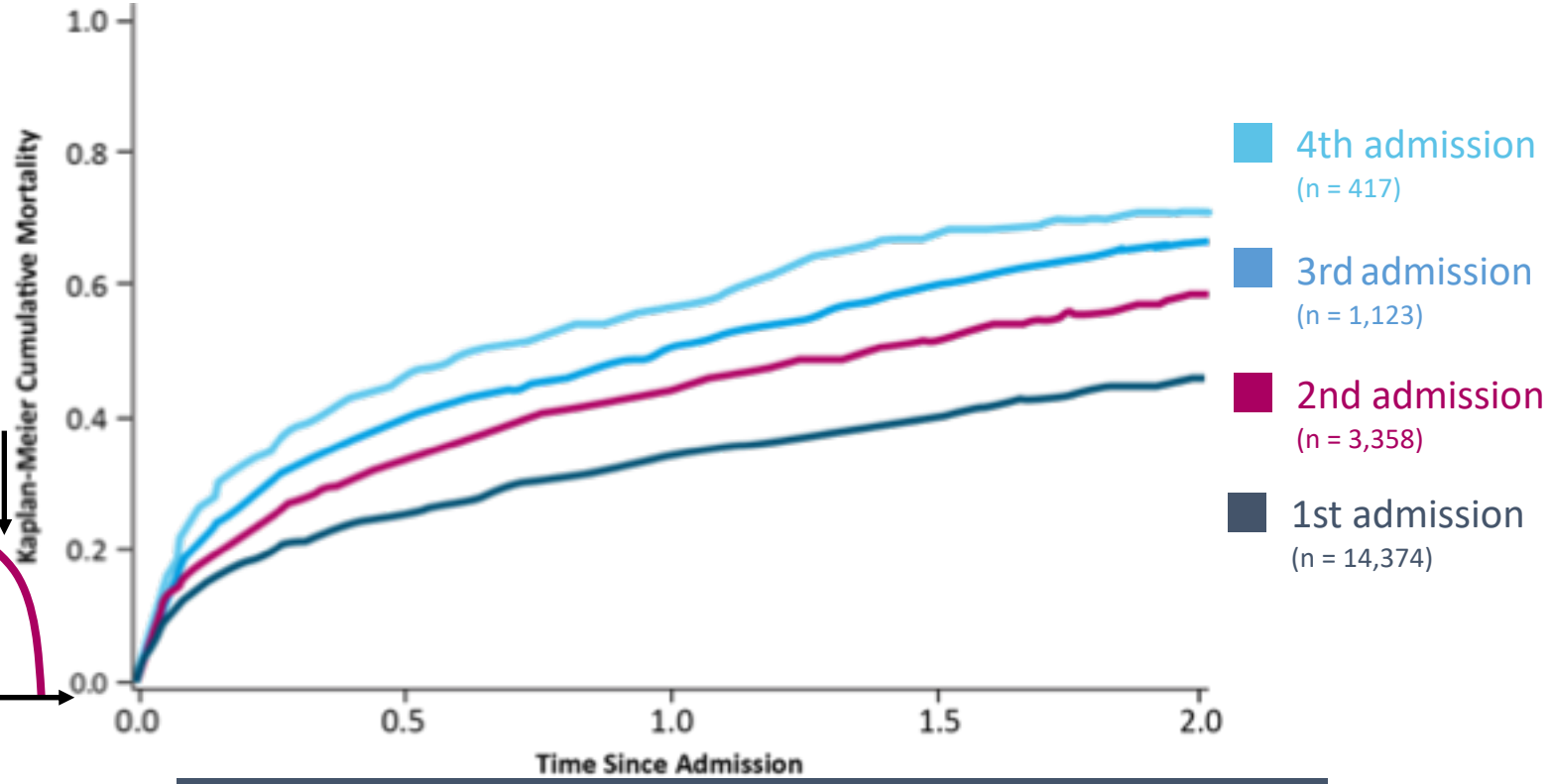
Lo Scompenso Cardiaco è un onere economico crescente

RICOVERI E RIAMMISSIONI		COSTI	
> 1,100,000 ricoveri per scompenso cardiaco[1]	**> 3,000,000** ricoveri che riportano lo scompenso cardiaco tra le cause.[2]	Per le spese mediche totali per lo scompenso cardiaco è previsto un **aumento a $70Mdi** entro il 2030, doppio rispetto al 2013.*	**50%** dei costi sono attribuiti ai ricoveri.[6]
~5 days durata media del ricovero[3]	**~25%** riammissione per qualsiasi causa entro 30 giorni; ~50% entro 6 mesi.[4,5]		

1. CDC. NCHS National Hospital Discharge Survey, 2000-10.
2. Blecker et al. *J Am Coll Cardiol*, 2013.
3. Yancy et al. *J Am Coll Cardiol*, 2006.
4. Wexler DJ, et al. *Am Heart J*, 2001.
5. Krumholz HM, et al. *Circ Cardiovas Qual Outcomes,* 2009.
6. Yancy CW, et al. *Circulation*, 2013.

Ogni evento acuto peggiora la prognosi del paziente

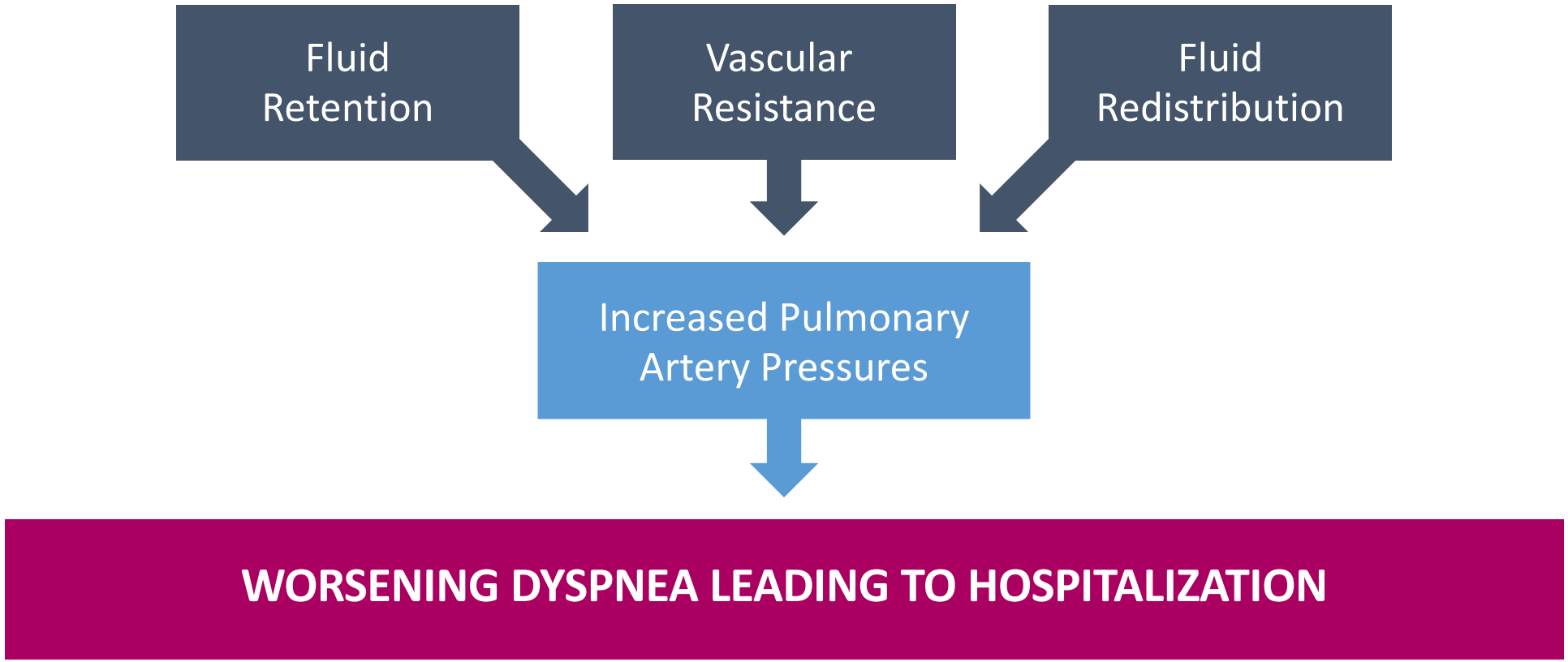




1. Gheorghiade MD, et al. *Am J. Cardiol*, 2005.

OBIETTIVO:
Controllare il volume per evitare episodi acuti di scompenso e ricoveri

Patogenesi delle riacutizzazioni di scompenso

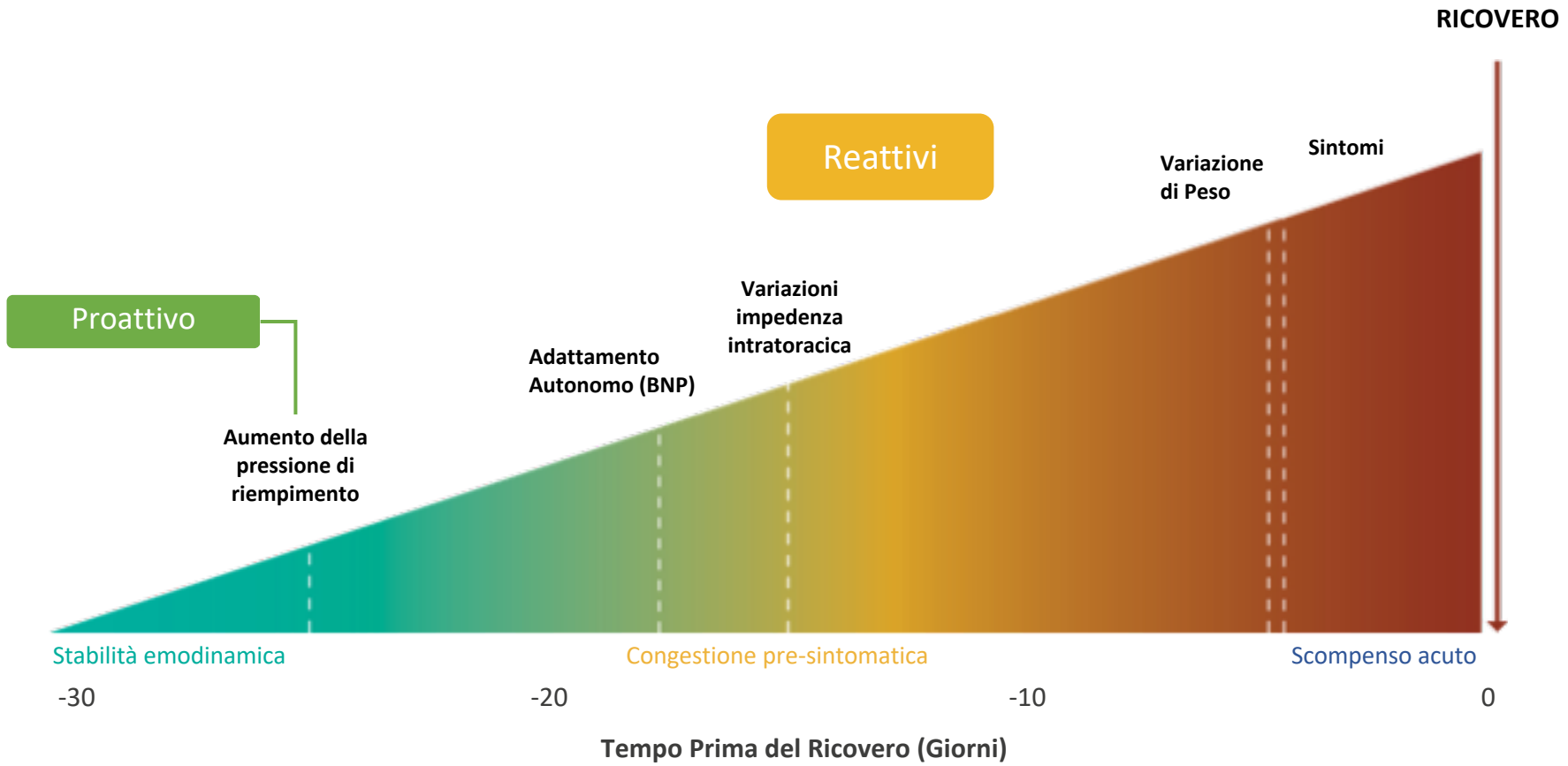


Gli strumenti attuali per valutare il grado di compenso

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

N = 366

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



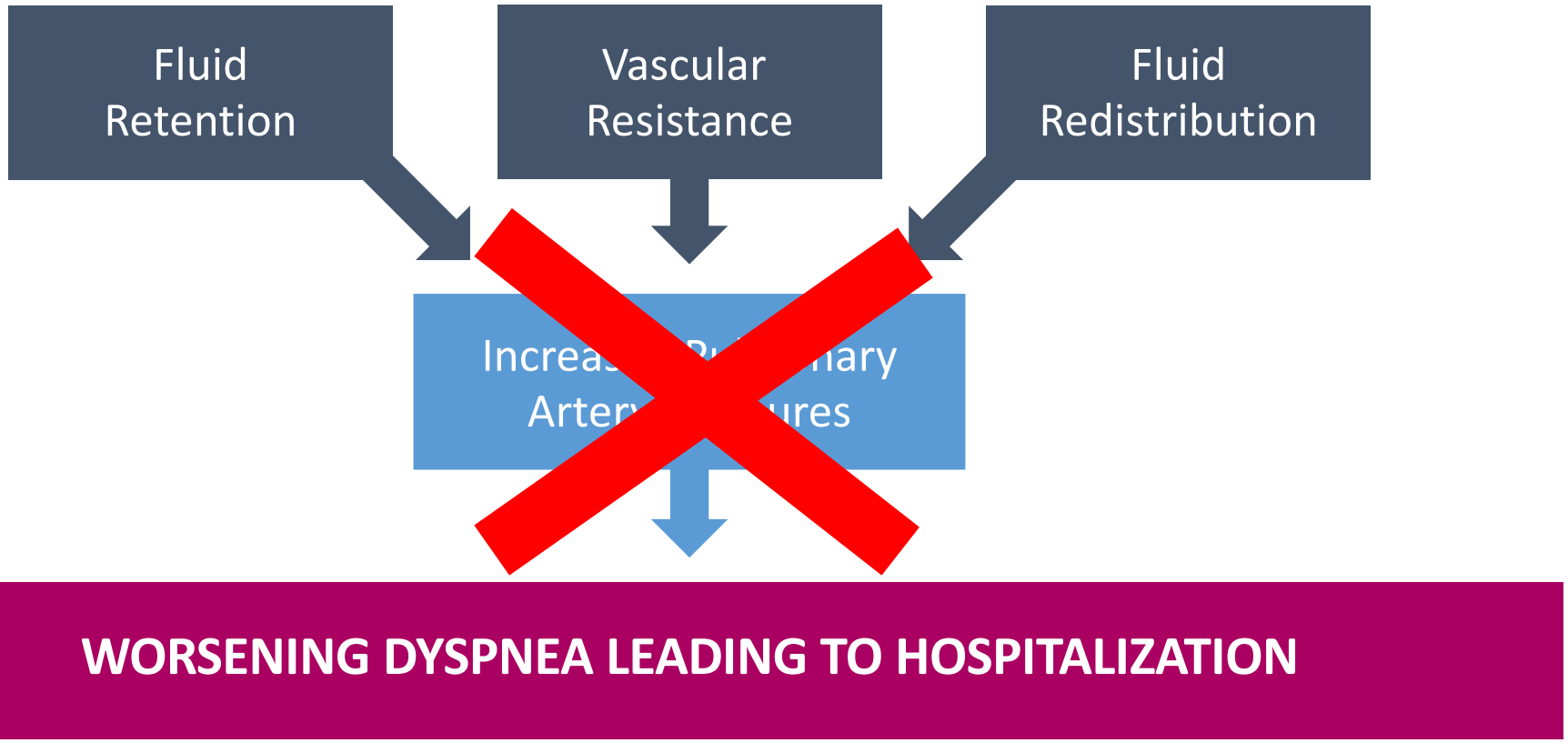
1. Adamson PB, et al. *Curr Heart Fail Reports*, 2009.

Ridotto impatto su ospedalizzazioni per scompenso

TRIAL	N	PARAMETER MONITORED	IMPACT ON HF HOSPITALIZATION	JOURNAL
TELE-HF[1]	1,653	Signs/symptoms, daily weights	None	*The New England Journal of Medicine, 2010*
TIM-HF[2]	710	Signs/symptoms, daily weights	None	*Circulation, 2011*
TEN-HMS[3]	426	Signs/symptoms, daily weights, BP, nurse telephone support	None	*Journal of the American College of Cardiology, 2005*
BEAT-HF[4]	1,437	Signs/symptoms, daily weights, nurse communications	None	*American Heart Association, 2016*
INH[5]	715	Signs/symptoms, telemonitoring, nurse coordinated DM	None	*Circulation Heart Failure, 2012*
DOT-HF[6]	335	Intrathoracic impedance with patient alert	Increased	*Circulation, 2011*
Optilink[7]	1,002	Intrathoracic impedance	None	*European Journal of Heart Failure, 2011*
REM-HF[8]	1,650	Remote monitoring via ICD, CRT-D or CRT-P	None	*European Society of Cardiology, 2017*
MORE CARE[9]	865	Remote monitoring of advanced diagnostics via CRT-D	None	*European Journal of Heart Failure, 2016*
Total	8,793	**MULTIPLE TRIALS, > 8,500 PATIENTS:** No reduction in HF hospitalization		

- 1. Chaudhry SI, et al. *N Engl J Med*, 2010.
- 2. Koehler F, et al. *Circulation*, 2011.
- 3. Cleland JG, et al. *J Am Coll Cardiol*, 2005.
- 4. Ong MK, et al. *JAMA Intern Med*, 2016.
- 5. Angermann DE, et al. *Circ Heart Fail*, 2012.
- 7. Brachmann J, et al. *Eur J Heart Fail*, 2011.
- 8. Cowie MR, *ESC,* 2016.
- 9. Boriani G, et al. *Eur J Heart Fail*, 2016.

Patogenesi delle riacutizzazioni di scompenso

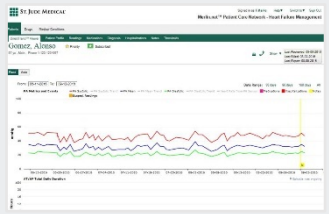


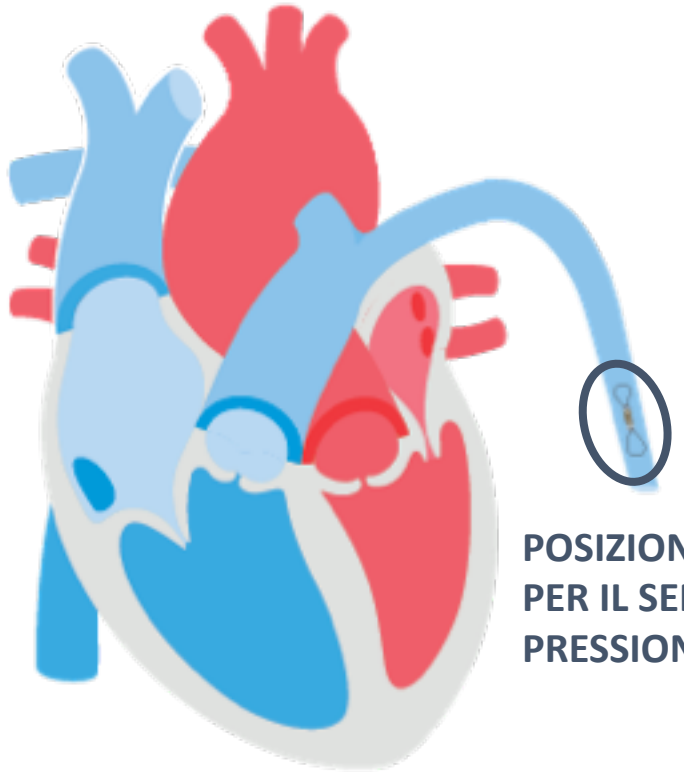
Il Sistema CardioMEMS™ HF

SENSORE DI PRESSIONE ARTERIOSA POLMONARE (PA)

SISTEMA ELETTRONICO PAZIENTE

MERLIN.NET™ PATIENT CARE NETWORK (PCN)





POSIZIONE TARGET PER IL SENSORE DI PRESSIONE PA

- 1. Abraham WT, *Lancet*, 2011.

Componenti del Sistema CardioMEMS™ HF

- PA Sensor

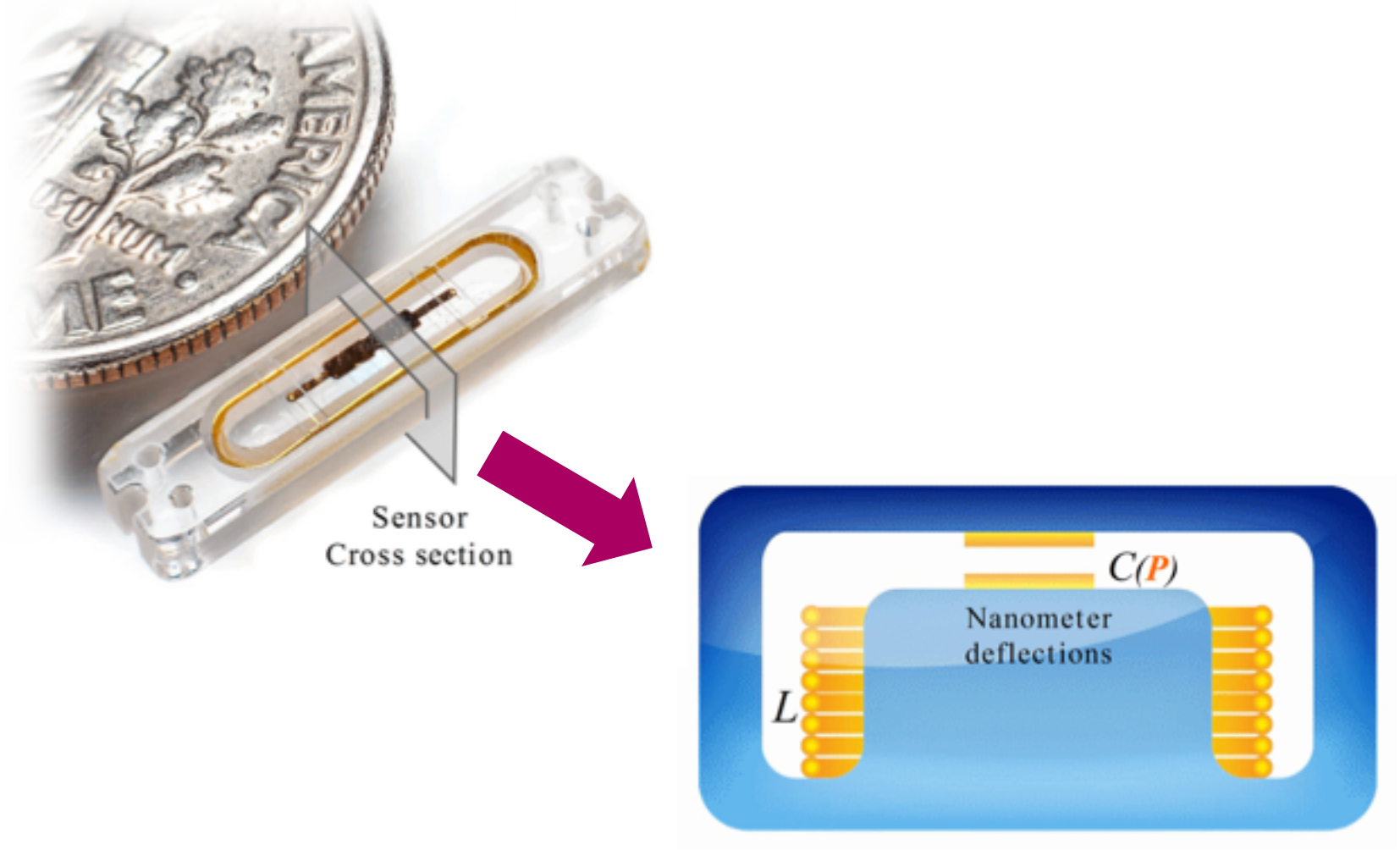
Over-the-wire Sensor Delivery System

Patient Electronics System

Hospital Electronics System

Microelectrical Mechanical System (MEMS)

No lead or battery, no need for replacement

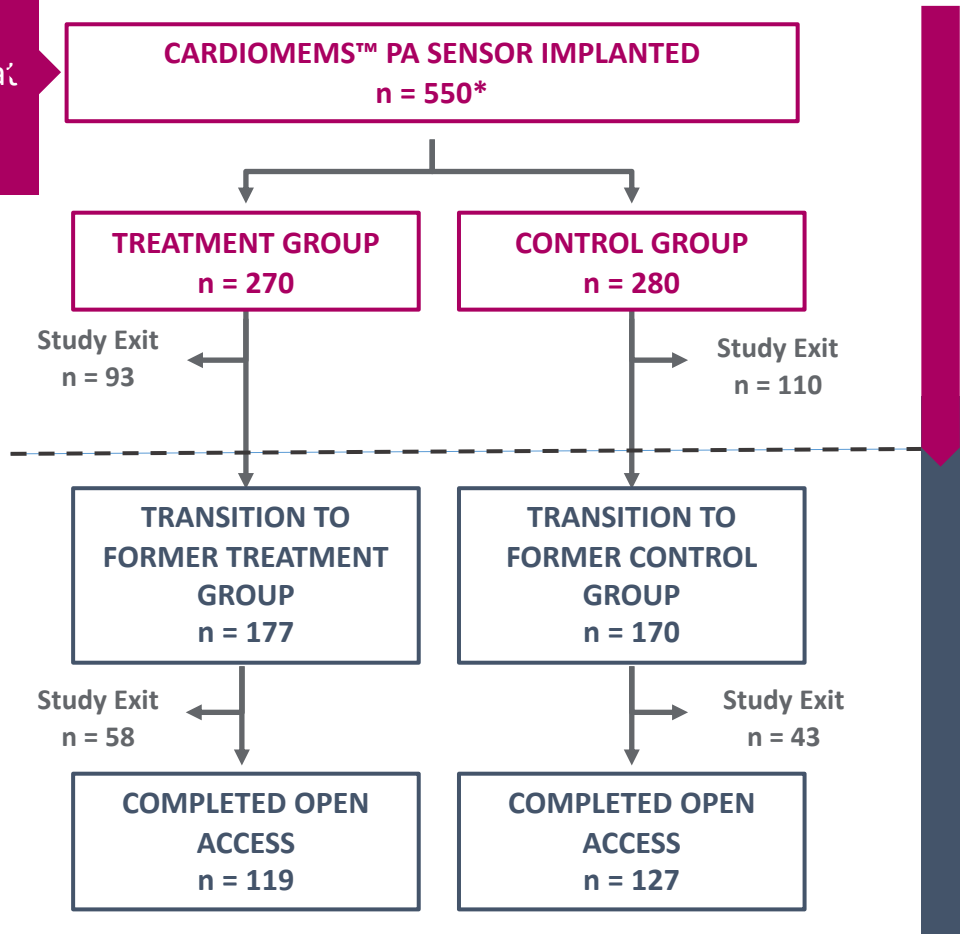



RESULTS

Il trial randomizzato CHAMPION

550 PREVIOUSLY HOSPITALIZED NYHA CLASS III PATIENTS

Previously hospitalized patients (past 12 months) with NYHA Class III HF for at least 3 months, regardless of LVEF



PART 1:
RANDOMIZED ACCESS[1]
18 MONTHS

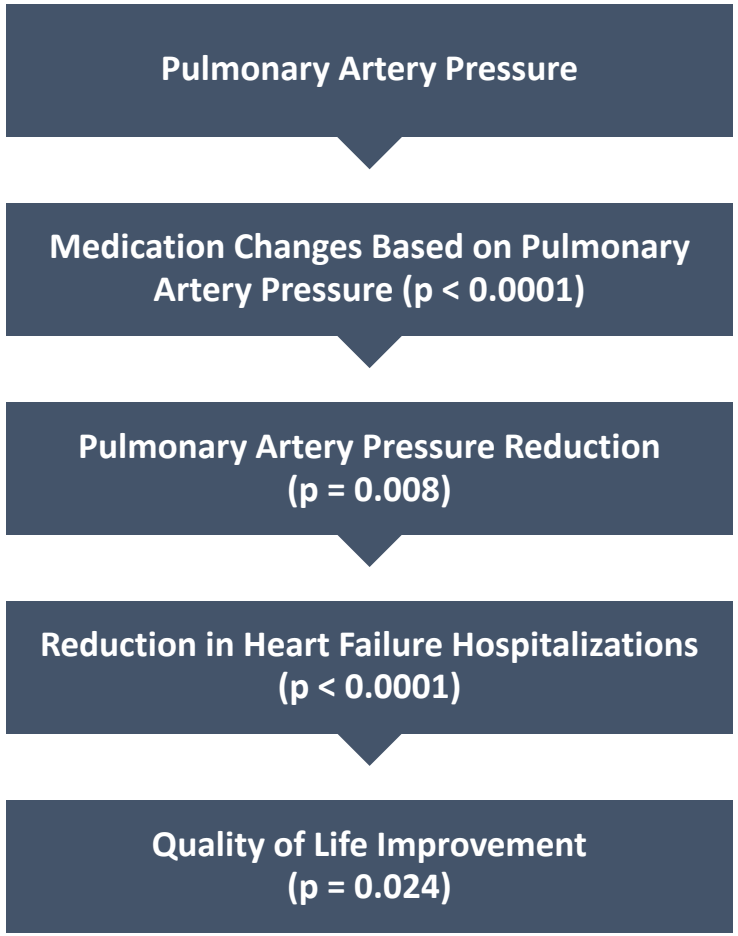
31 MONTHS AVERAGE FOLLOW-UP

PART 2:
OPEN ACCESS[2]
13 MONTHS

- *575 consented. 25 could not be implanted due to anatomy, comorbidities, etc. All took daily readings.
- 1. Abraham W, et al. *Lancet*, 2011.
- 2. Abraham W, et al. *Lancet*, 2016.

Il trial randomizzato CHAMPION

550 PREVIOUSLY HOSPITALIZED NYHA CLASS III PATIENTS



1. Abraham WT, et al. *Lancet*, 2011.
2. Abraham WT, et al. *Lancet*, 2016.
3. Adamson PB, et al. *J Card Fail*, 2010.

MANAGING PRESSURES TO TARGET GOAL RANGES:

- PA pressure systolic 15–35 mmHg
- PA pressure diastolic 8–20 mmHg
- PA pressure mean 10–25 mmHg

Terapia guidata dalla Pressione Polmonare

Il trial randomizzato CHAMPION

550 PREVIOUSLY HOSPITALIZED NYHA CLASS III PATIENTS

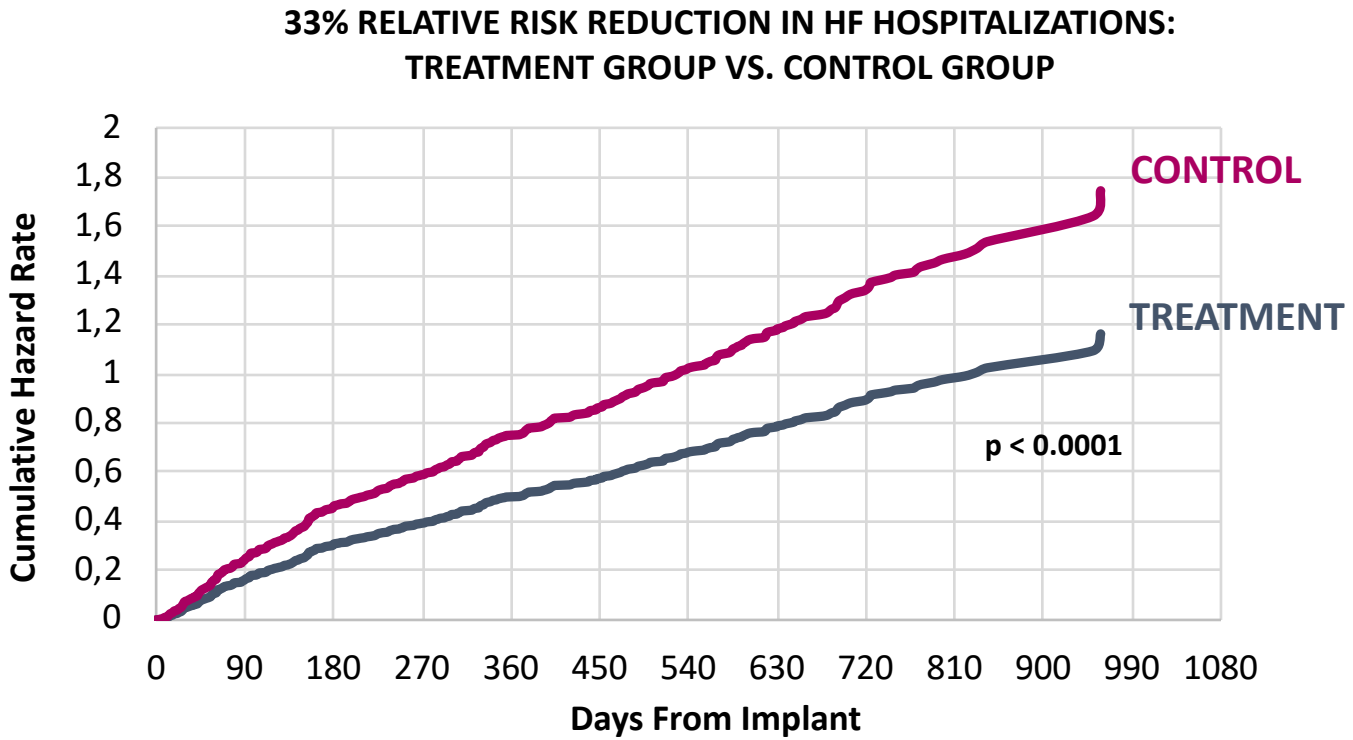
	Not enrolled (n=25)	Treatment group (n=270)	Control group (n=280)	All patients (n=575)	Risk (95% CI)	p value	NNT
Primary efficacy endpoints*							
Heart-failure-related hospitalisations up to 6 months (number; events per patient per 6 months)	NA	84 (0·32)	120 (0·44)	NA	0·72† (0·60–0·85)	0·0002	8
Primary safety endpoints‡							
Device-related or system-related complications	2 (8%)	3 (1%)	3 (1%)	8 (1%)	§	<0·0001	NA
Pressure-sensor failures	0	0	0	0	§	<0·0001	NA
Prespecified supplementary efficacy endpoints¶							
Heart-failure-related hospitalisations during entire randomised follow-up	NA	158	254	NA	0·63† (0·52–0·77)	<0·0001	4
Secondary efficacy endpoints							
Change from baseline in pulmonary artery mean pressure at 6 months (mm Hg×days; mean area under the curve)	NA	−156	33	NA	NA	0·008	NA
Patients admitted to hospital for heart failure at 6 months	NA	55 (20%)	80 (29%)	NA	0·71‖ (0·53–0·96)	0·03	NA
Days alive outside hospital at 6 months (mean, SD)	NA	174·4 (31·1)	172·1 (37·8)	NA	NA	0·02	NA
Minnesota Living with Heart Failure Questionnaire at 6 months (mean, SD)	NA	45 (26)	51 (25)	NA	NA	0·02	NA

Data are number (%) or number, unless otherwise indicated. NNT=number needed to treat. NA=not applicable. *p value from negative binomial regression for comparison of treatment group with control group. †Hazard ratio. ‡p value from exact test of binomial proportions of freedom from events compared with 80% (device-related or system-related complications) and 90% (pressure sensor failure) for all patients. §Risk difference not reported because analysis by randomisation group was not prespecified. ¶p value from the Anderson-Gill model for comparison of treatment group with control group. ‖Relative risk.

Table 2: **Effect of wireless implantable haemodynamic monitoring on safety and efficacy endpoints**

End-point primario - Efficacia

- **PART 1: RANDOMIZED ACCESS**



No. at Risk												
CONTROL	280	267	254	241	210	175	131	101	62	27	12	5	0
TREATMENT	270	262	246	235	197	164	125	105	75	38	8	3	0

- Abraham W, et al. *Lancet*, 2016.

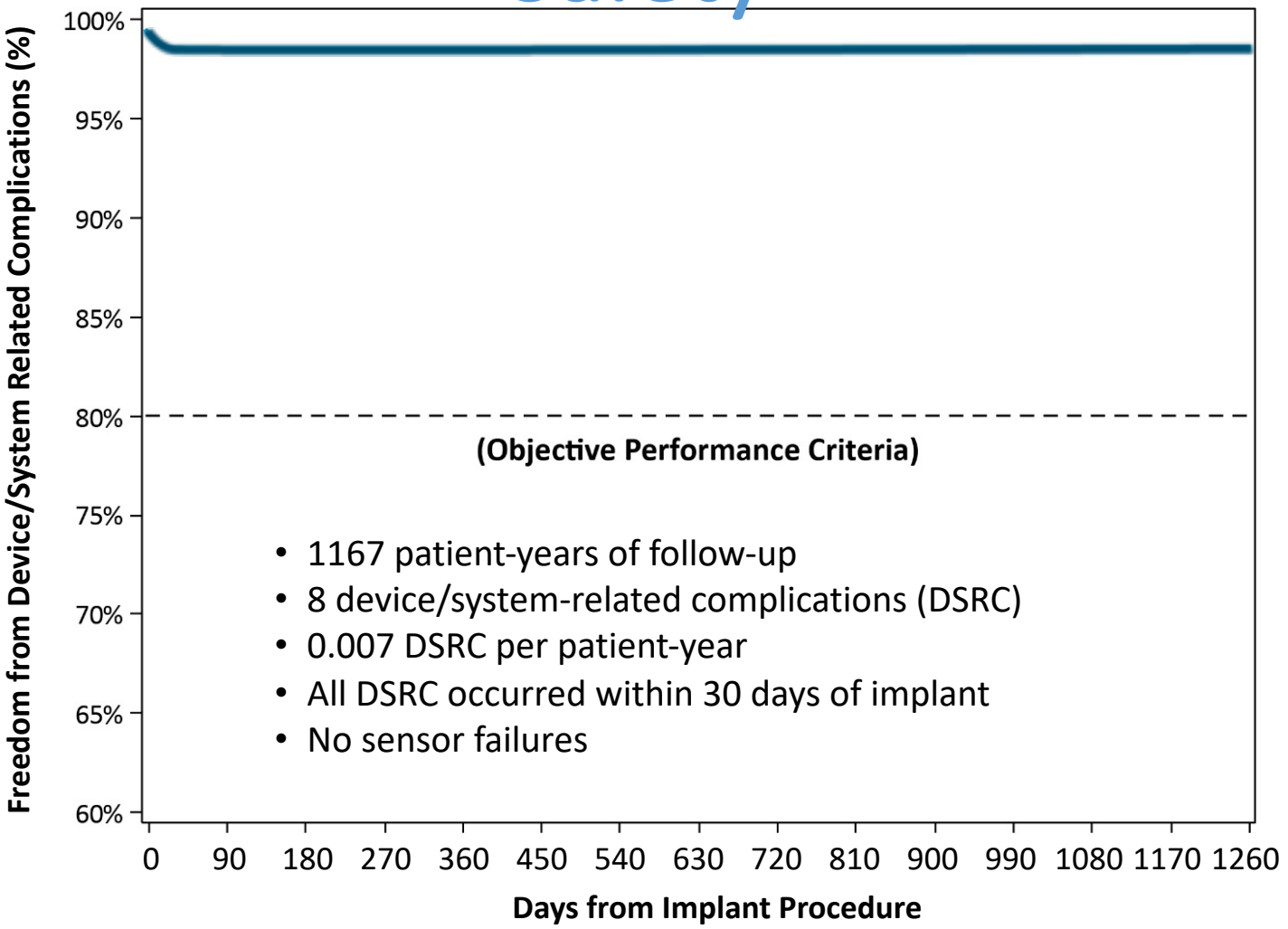
End-points secondari

PART 1: RANDOMIZED ACCESS

		TREATMENT (N = 270)	CONTROL (N = 280)	P-VALUE
SECONDARY ENDPOINTS	Change from baseline in PA mean pressure (mean AUC [mmHg x days])	-156	33	0.008
	Number and proportion of patients hospitalized for HF (%)	55 (20%)	80 (29%)	0.03
	Days alive and out of hospital for HF (mean ± SD)	174.4 ± 31.1	172.1 ± 37.8	0.02
	Quality of life (Minnesota Living with Heart Failure Questionnaire, mean ± SD)	45 ± 26	51 ± 25	0.02

- *Total of 8 DSRCs including 2 events in Consented not implanted patients (n = 25)
- Abraham WT, et al. *Lancet*, 2011.

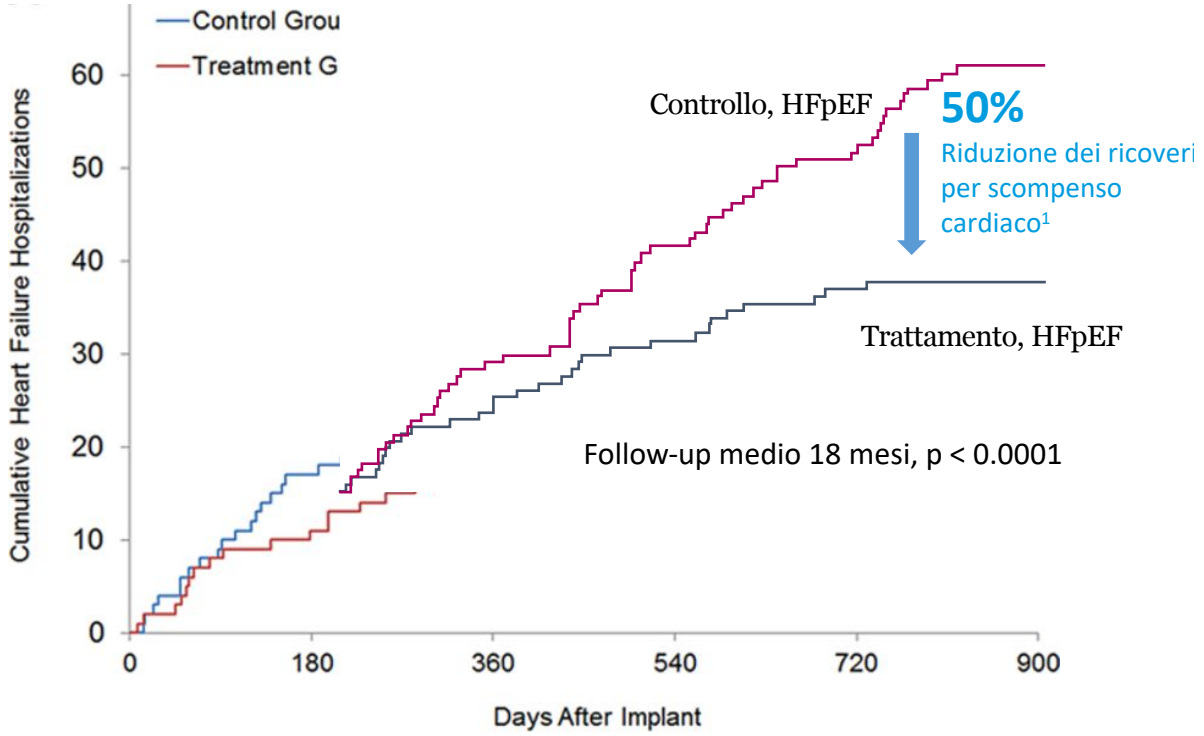
Safety



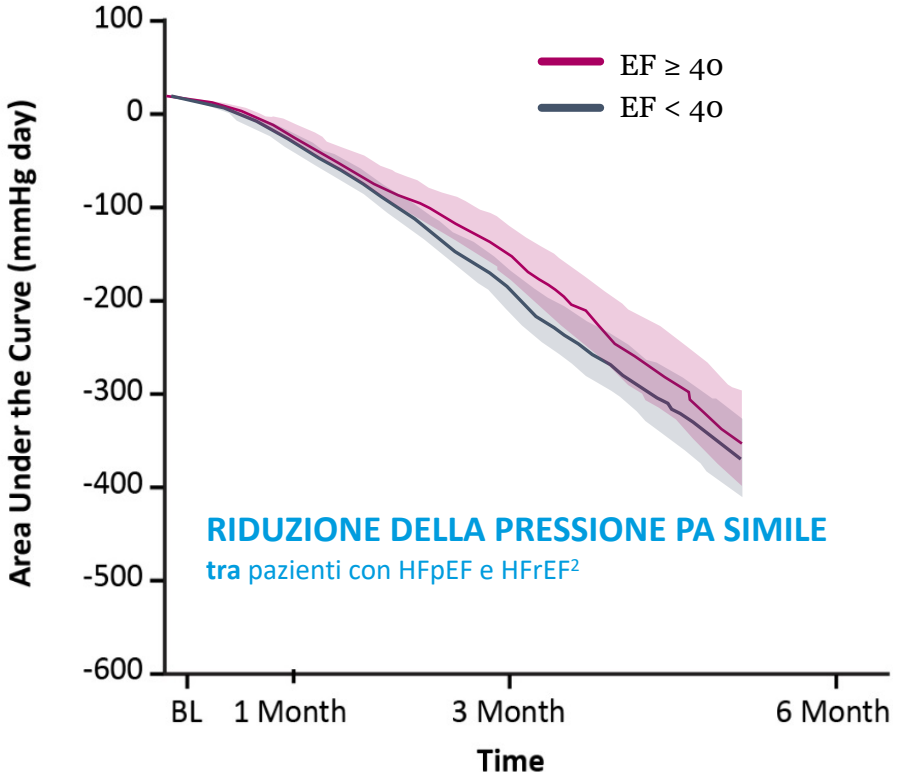
No. at Risk	570	525	497	474	446	420	395	363	326	300	283	253	127	10	1

Efficacia del sistema CardioMEMS™ HF nella popolazione HFpEF

RIDUZIONE DEI RICOVERI PER SCOMPENSO CARDIACO



RIDUZIONE DELLA PRESSIONE PA action



1. Jermyn R, et al. Clinical Cardiology. doi: 10.1002/clc.22643.
2. Heywood JT, Jermyn R, Shavelle D, et al. Circulation 2017;135: 1509–17.
3. Adamson PB, et al. Circ Heart Fail, 2014 Nov;7(6):935-44.

The CHAMPION Trial Subgroup Analyses:

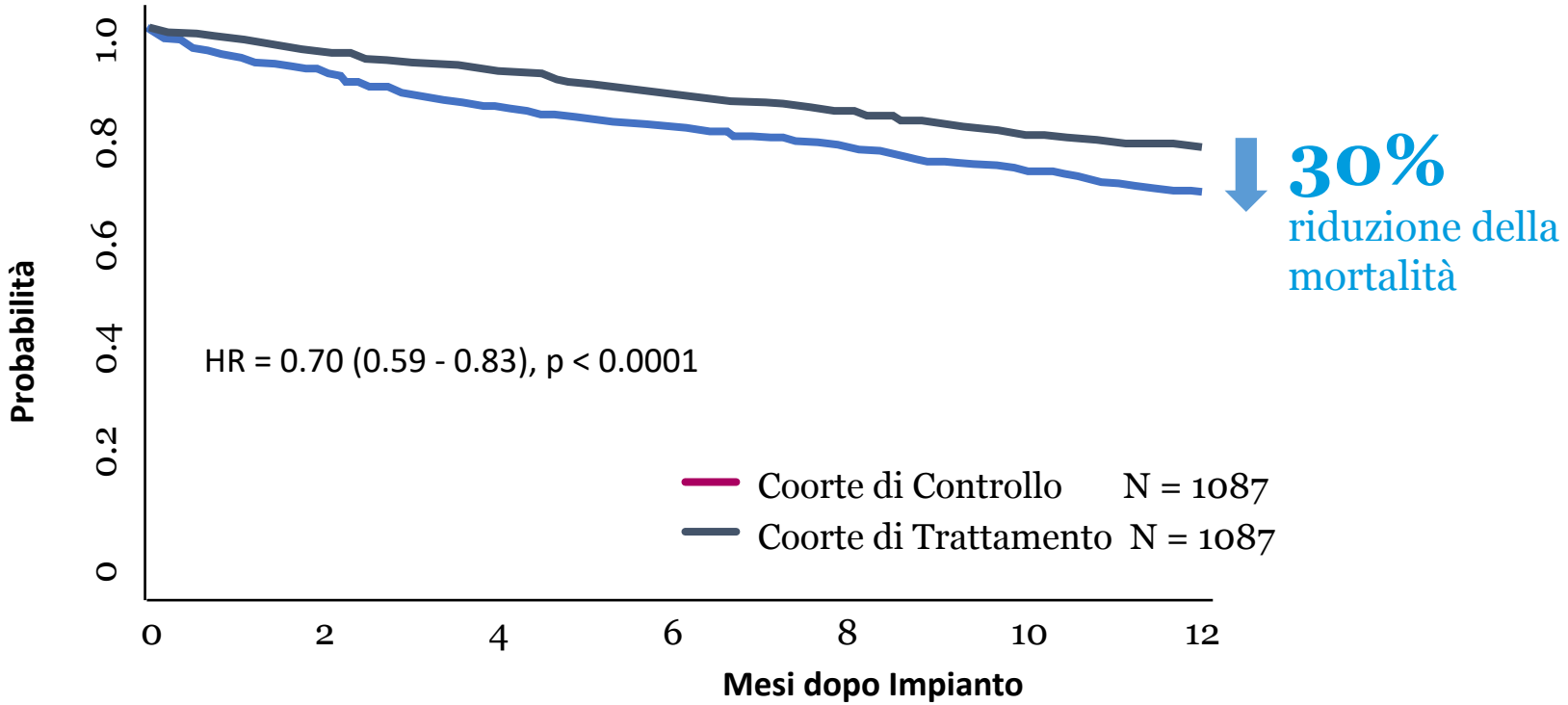
REDUCTION OF HF HOSPITALIZATION IN PATIENT GROUPS WITH COMMON COMORBIDITIES

Sub-Group or Comorbidity	n (control)	n (treatment)	Follow-up Period (months)	Reduction of HF Hospitalization Rate in Treatment Group vs. control
Medicare population[1]	125	120	18	49%, $p < 0.0001$
HFpEF[2]	56	59	18	50%, $p < 0.0001$
HFrEF following GDMT[3]	174	163	17	43%, $p < 0.0001$
CRT-D or ICD following GDMT[4]	146	129	18	43%, $p < 0.0001$
History of myocardial infarction[5]	137	134	15	46%, $p < 0.001$
COPD[6,7]	96	91	15	41%, $p = 0.0009$
Pulmonary hypertension[8]	163	151	15	36%, $p = 0.0002$
AF[9]	135	120	15	41%, $p < 0.0001$
Chronic kidney disease[10]	150	147	15	42%, $p = 0.0001$

Patients with common HF comorbidities and patients in important subgroups
HAVE CONSISTENT REDUCTION IN HF HOSPITALIZATIONS with PA pressure-guided therapy.

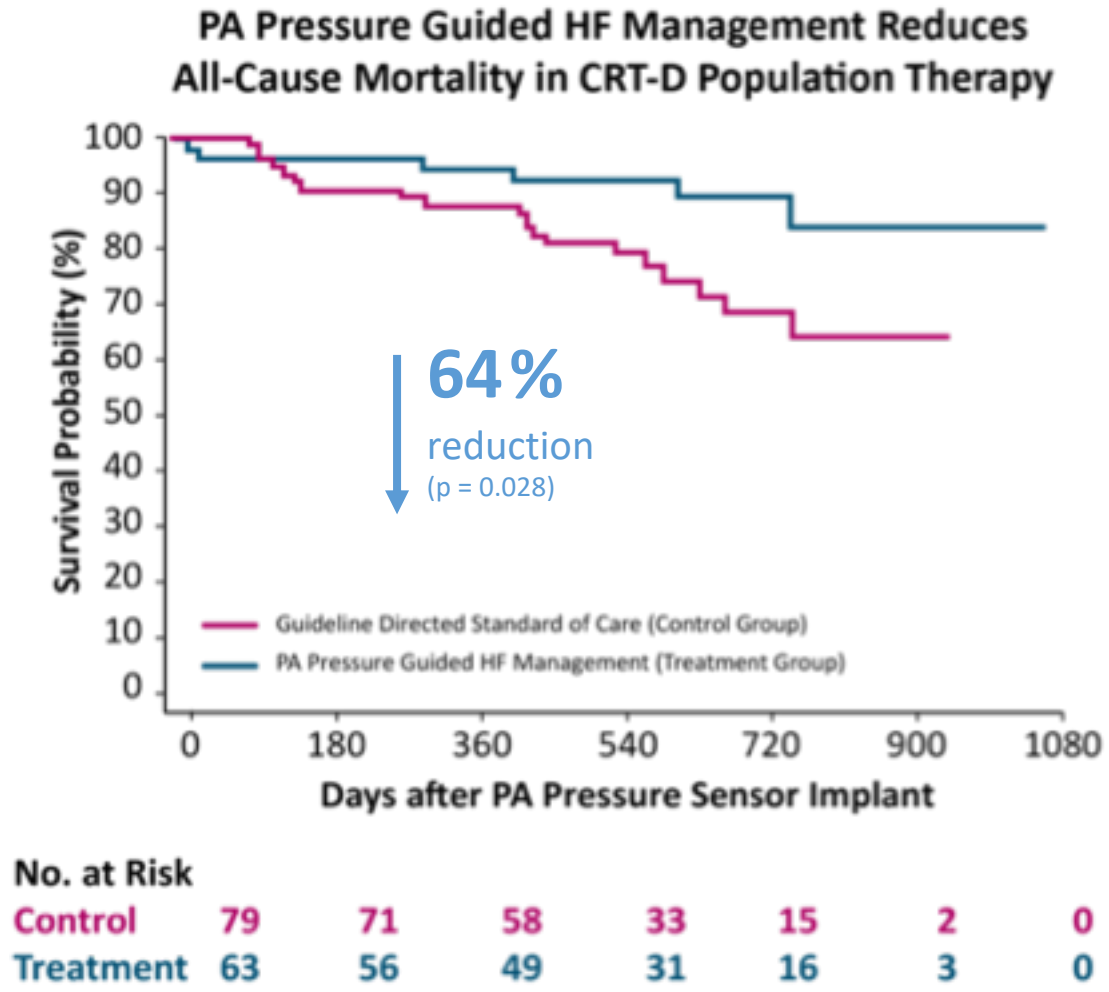
1. Adamson, et al. *Circ Heart Fail*, 2016.
2. Adamson, et al. *Circ Heart Fail*, 2014.
3. Abraham, et al. *ACC*, 2015.
4. Abraham, et al. *HRS* 2015.
5. Strickland WL, et al. *J Am Coll Cardiol*, 2011.
6. Criner G, et al. *Eur Respir J*, 2012.
7. Martinez F, et al. *Eur Respir J*, 2012.
8. Benza R, et al. *J Card Fail*, 2012.
9. Miller AB, et al. *J Am Coll Cardiol*, 2012.
10. Abraham, et al. *J Card Fail*, 2014.

Riduzione significativa della mortalità in studio retrospettivo



1. Abraham, et al. Presented at ACC 2018

Pazienti con CRT



Abraham, et al. *HRS* 2015.

NNT

- **PART 1: RANDOMIZED ACCESS**

INTERVENTION	TRIAL	MEAN DURATION OF RANDOMIZED FOLLOW-UP	ANNUALIZED REDUCTION IN HF Hospitalization RATES	NNT/YEAR TO PREVENT 1 HF HOSPITALIZATION
Beta-blocker[1]	COPERNICUS	10 months	33%	7
Aldosterone antagonist[2]	RALES	24 months	36%	7
CRT[3]	CARE-HF	29 months	52%	7
Beta-blocker[4]	MERIT-HF	12 months	29%	15
ACE inhibitor[5]	SOLVD	41 months	30%	15
Aldosterone antagonist[6]	EMPHASIS-HF	21 months	38%	16
Digoxin[7]	DIG	37 months	24%	17
Angiotensin receptor blocker[8]	Val-HeFT	23 months	23%	18
Angiotensin receptor blocker[9]	CHARM	40 months	27%	19
PA pressure monitoring[10]	CHAMPION	18 months	33%	**4**

PA pressure monitoring led to lower NNT
to prevent one hf-related hospitalization vs. other therapies

- 1. Packer M, et al. *Circulation,* 2002.
- 2. Pitt B, et al. *N Engl J Med,* 1999.
- 3. Cleland JG, et al. *N Engl J Med,* 2005.
- 4. Hjalmarson A, et al. *JAMA*, 2000.
- 5. The SOLVD Investigators. *N Engl J Med*, 1991.
- 6. Zannad F, et al. *N Engl J Med*, 2011.
- 7. Digitalis Investigation Group. *N Engl J Med*, 1997.
- 8. Cohn JN, et al. *N Engl J Med*, 2001.
- 9. Young JB, et al. *Circulation,* 2004.
- 10. Adamson, P. et al. *HFSA,* 2016.

Miglioramento 6 MWT

*Il Sistema CardioMEMS™ HF ha aumentato la 6MWD di 54.5 m vs. il gruppo standard of care,[1] $p < 0.005$

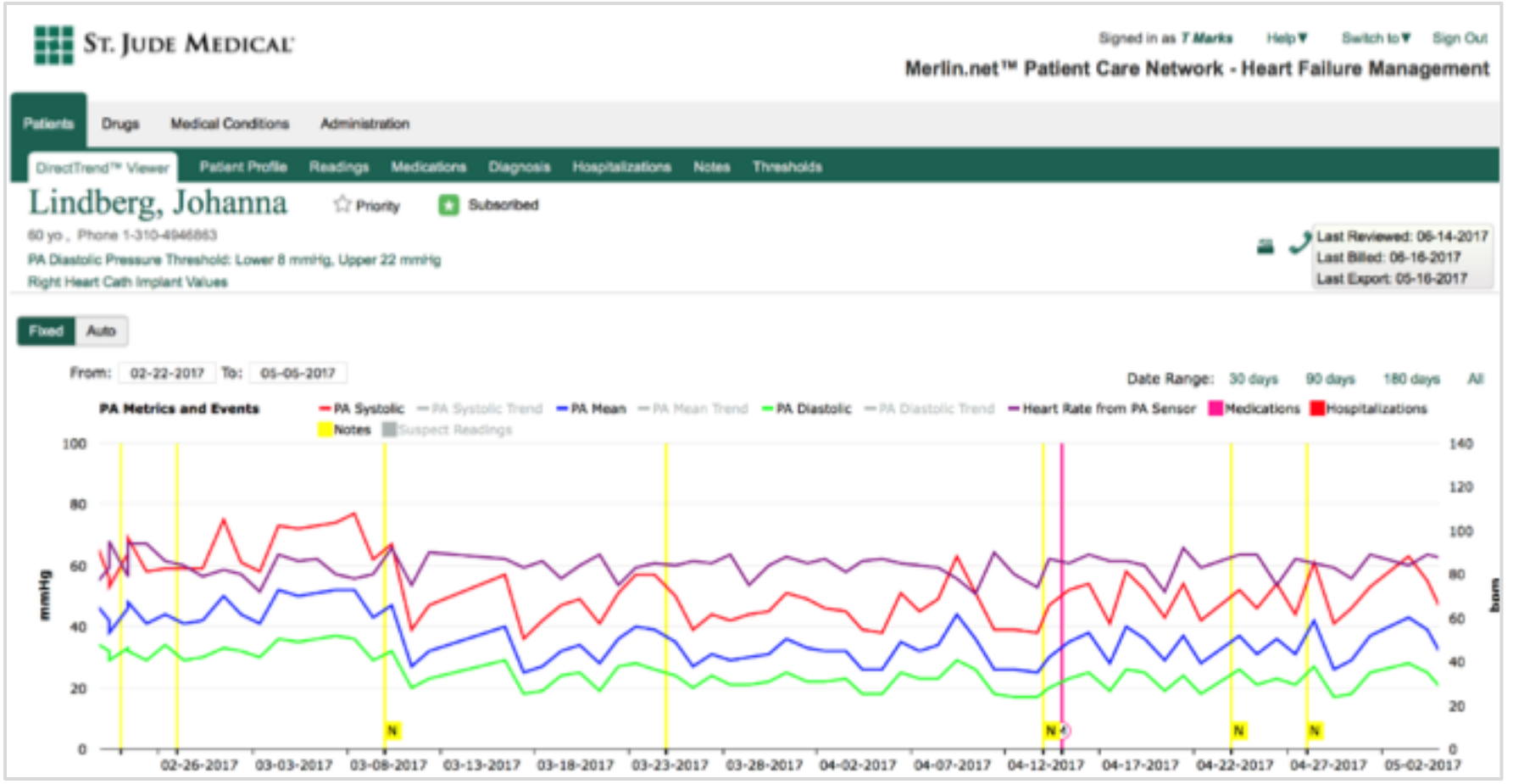
1. Jermyn R, et al. *Clinical Cardiology.* doi: 10.1002/clc.22643.

Miglioramento della qualità della vita

PUNTEGGIO A 12 MESI
Minor Punteggio = Miglior QoL

1. Abraham WT, et al. *The Lancet, 387*(10017), 453-461.
2. American Thoracic Society. Accessed August 22, 2016.

Interfaccia



DirectTrend™ Viewer è personalizzabile per vedere
TREND SPECIFICI PER OGNI PAZIENTE

Conclusioni:

Il monitoraggio della pressione arteriosa polmonare è un sistema affidabile per la valutazione del compenso emodinamico del pz, sia con frazione di eiezione ridotta che conservata

Esso permette un approccio alla terapia precoce e «pro-attivo», con documentata riduzione delle ospedalizzazioni per scompenso e miglioramento della sopravvivenza rispetto allo SOC


Grazie per
l’ attenzione!