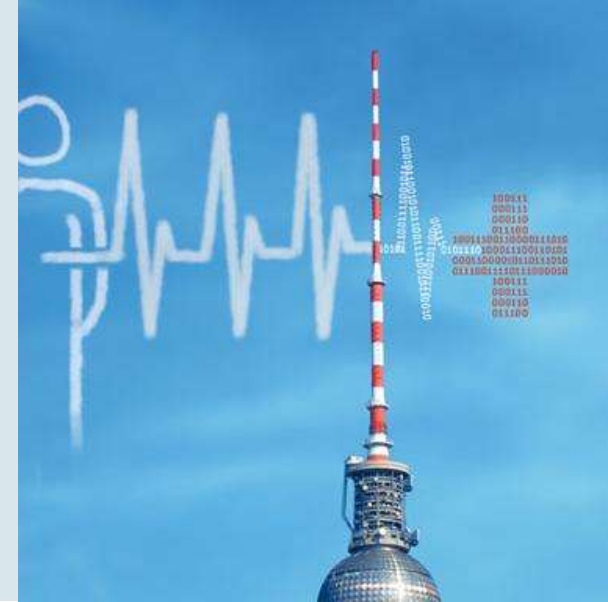


A randomized controlled trial: Telemedical Interventional Monitoring in Heart Failure (TIM-HF)



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Heart Failure Congress 2011, Gothenburg

Late Breaking Trials

22 May 2011



Partnership for the Heart

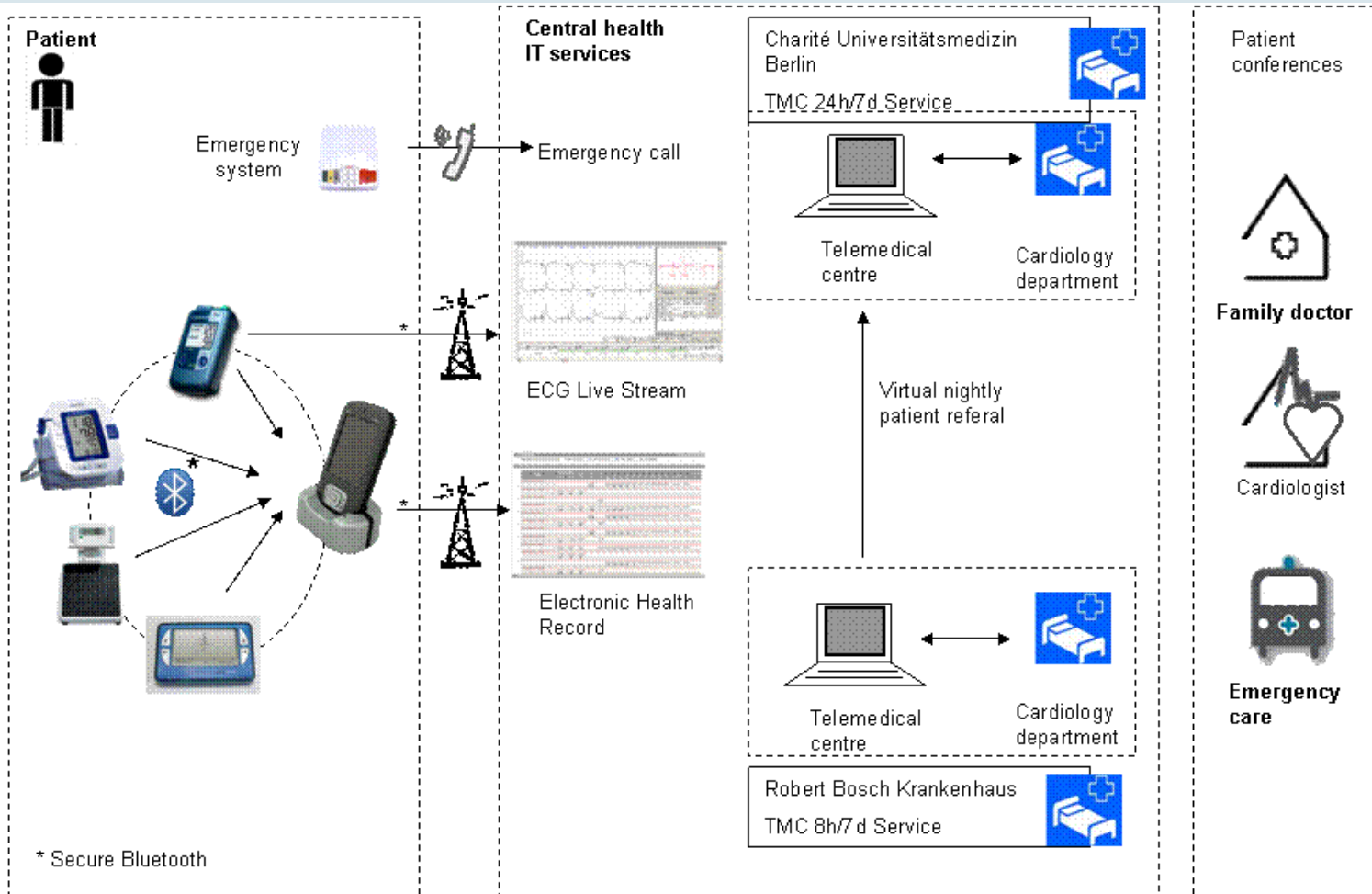


- Part of the research and development programme „next generation media, sponsored by the German Federal Ministry of Economics and Technology (Project No.: 01MG531)
- Development of a Remote Patient Monitoring System including Mobile Sensor Platform and Electronic Patient Record for the Telemedical Monitoring of Heart Failure Patients
- RCT-Trial: „Telemedical Interventional Monitoring in Heart Failure (TIM-HF)“ (NCT00543881)

Facts:

- Federal Grant: 7.15 Mio €
- Total Volume: 16.2 Mio €
- Project Duration: 2005-2011
- Clinical Trial (TIM-HF): 01'08 - 06'10

The Remote Telemedical System used in TIM-HF



Koehler et al. *Circulation* 2011

Study Design

Randomisation of 710 patients

- 354 (49,9%) Remote patient monitoring + guideline based therapy (RTM)
- 356 (50,1%) guideline based therapy (control group, UC)

Main inclusion criteria:

- NYHA class II / III, LVEF \leq 35%
- Decompensation due to HF in prior 24 months or LVEF \leq 25%
- Considered optimally treated (i.e. ACEi/ARB, Beta-Blocker & diuretic)

Main exclusion criteria:

- Hospitalization for worsening HF within previous 7 days
- Planned CRT implantation

Compliance to telemedical care & follow-up:

- Definition: \geq 70% of possible daily transfers (excl hospitalizations) and no “break” >30 days -- this was achieved by 287 (81%) of 354 RTM pats
- Completeness of follow-up: 99.7%

Blinding:

- Clinical Endpoint Committee: all unplanned hospitalizations were adjudicated using pre-defined criteria (see design paper)

Baseline Characteristics (I/II)

	RTM (N=354)	Usual Care (N=356)
Age (years)	67	67
Gender (% male)	81	82
Ischemic etiology (%)	57	55
ICD (%)	46	45
LVEF (%)*	27±6	27±6
Diabetes (%)	40	39
ACEi/ARB (%)	97	94
Beta-Blocker (%)	92	93
Diuretic (%)	94	94
Aldosterone antagonist (%)	65	63
NYHA class II (%)	50	51
NYHA class III (%)	50	49

*mean ± SD

Baseline Characteristics (II/II)

	RTM (N=354)	Usual Care (N=356)
Living alone (%)	21	22
SBP (mm Hg)*	121 ± 16	122 ± 16
DBP (mm Hg)*	74 ± 10	74 ± 10
PHQ-9 depression score*	6.4 ± 4.4	6.6 ± 4.6
SF-36 Physical Functional score*	51 ± 26	51 ± 26
Creatinine (µmol/L)*	115 ± 37	111 ± 31
Estimated GFR (mL/min/1.73m ²)*	63 ± 22	64 ± 20
Uric acid (µmol/L)*	448 ± 128	442 ± 114
Duration of heart failure, y	6.7 ± 6.6	6.8 ± 6.4

*mean ± SD

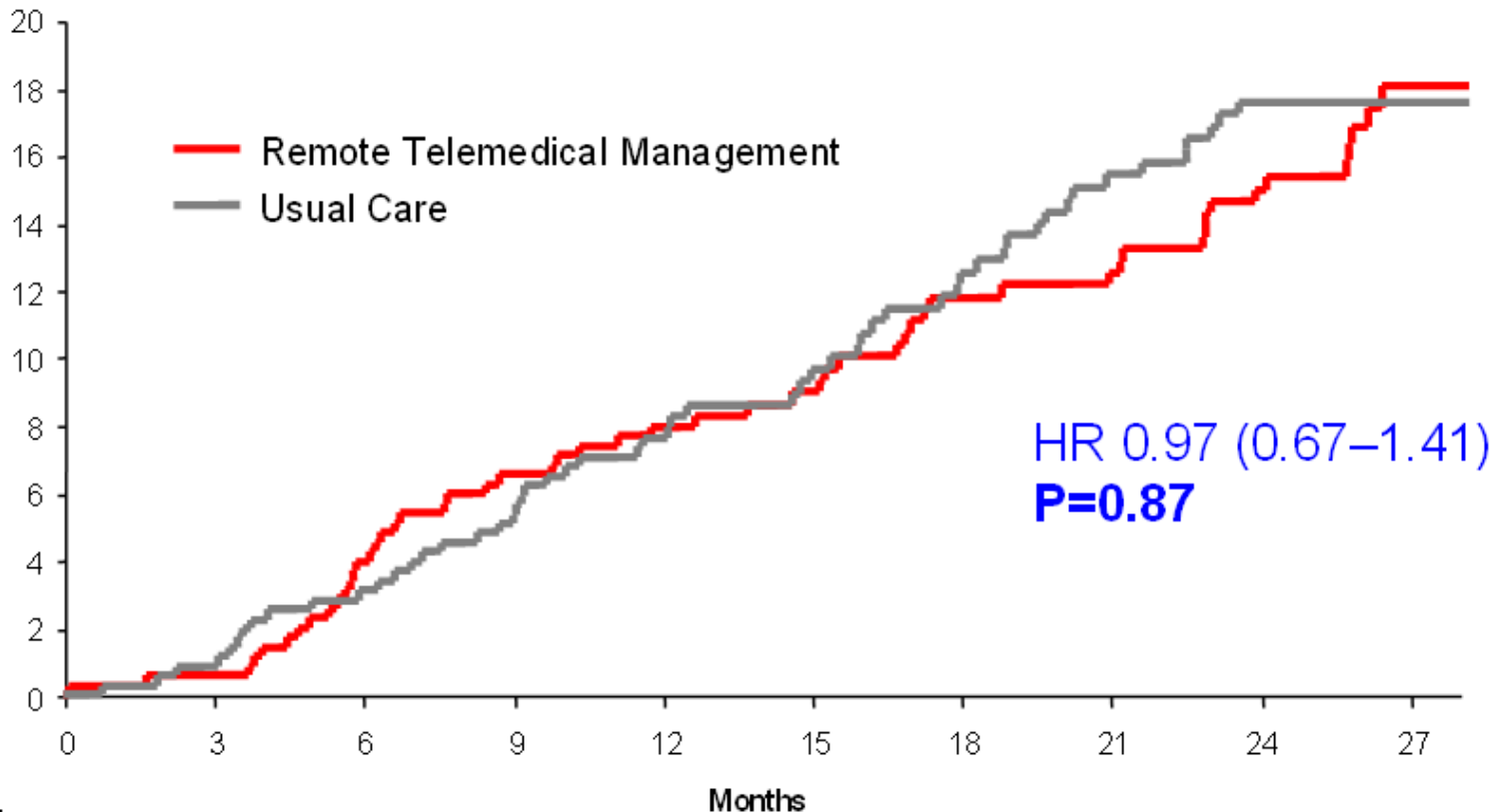
Primary and secondary endpoints

- **Primary**
 - Total mortality
- **Key secondary**
 - Composite of CV death & hospitalization for HF
 - Days lost due to death or hospitalization for HF
 - CV mortality
 - Duration of HF hospitalizations
 - Rate of CV & of HF hospitalizations at 6, 12 & 24 months
 - NYHA class, SF-36 physical functioning score & PHQ-9 depression score at 12 & 24 months*

* Adjusted for baseline

Primary Endpoint: All-cause Mortality

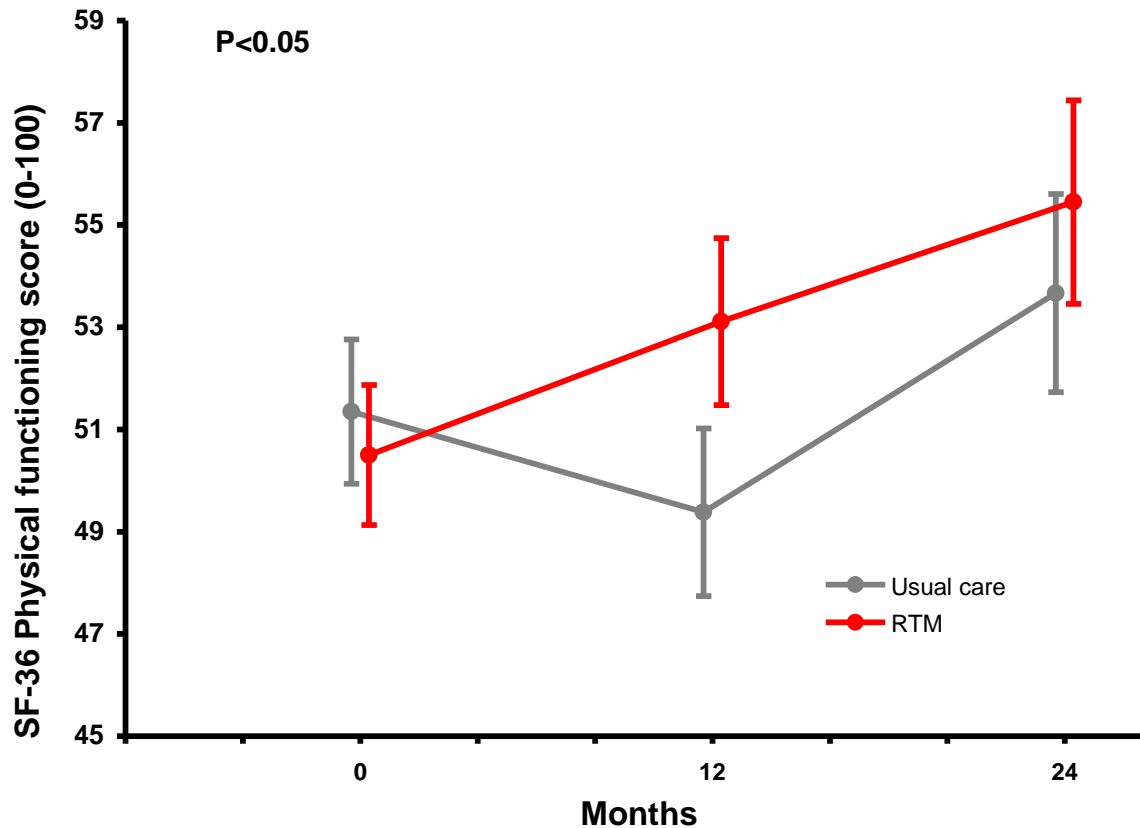
Proportion of patients with event (%)



Patients at risk

	0	3	6	9	12	15	18	21	24	27
RTM	354	352	340	330	307		249		239	64
Usual Care	356	352	344	336	305		243		229	60

Second Endpoint: SF-36 Physical functioning score

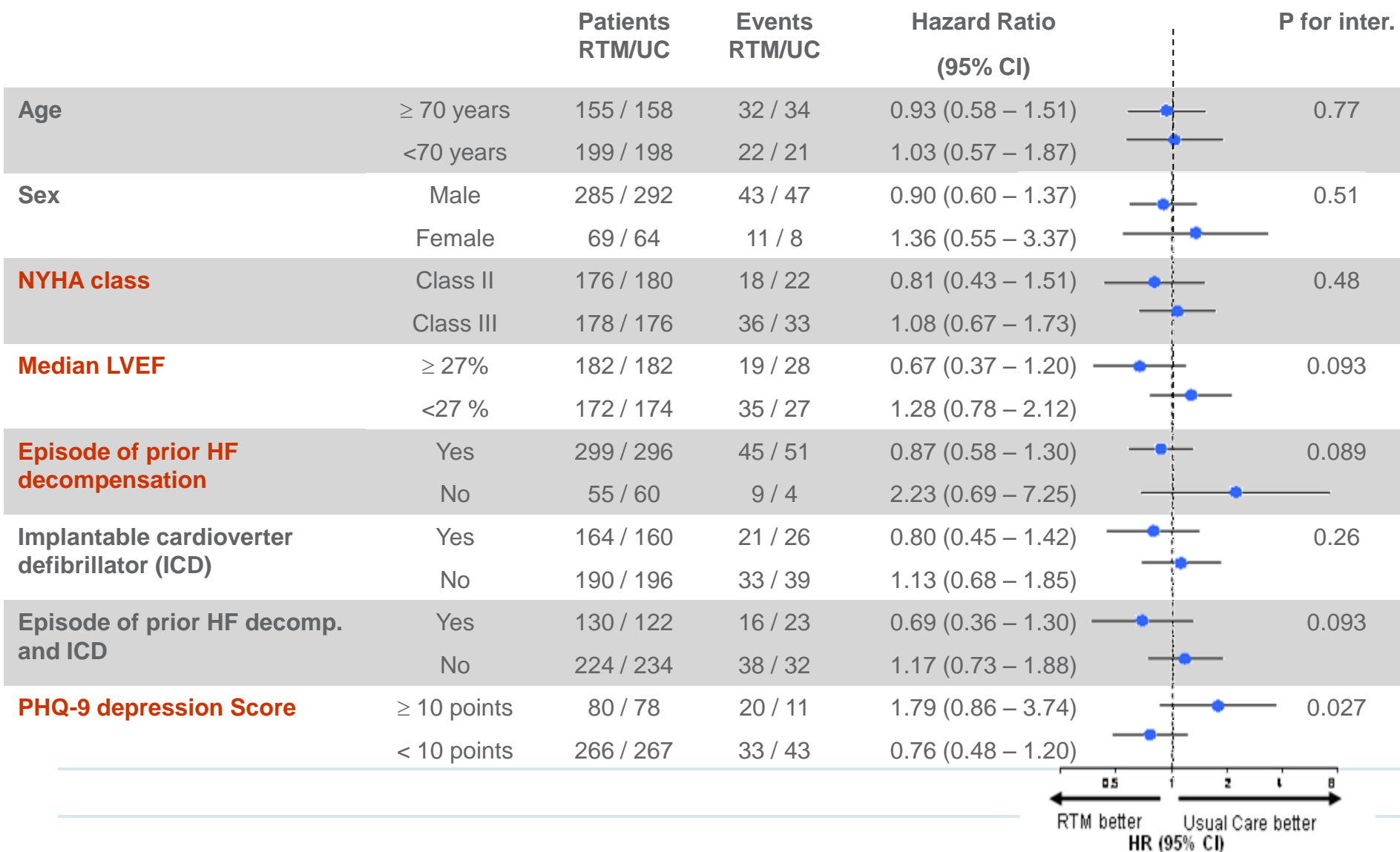


No. of score available

RTM	348	294	207
Usual care	350	295	205

Koehler et al., *Circulation* 2011

Predefined Subgroup Analysis: total mortality



Predefined Subgroup Analysis: days lost due to death or HF hospitalization



		RTM (N=354)	UC (N=356)	P Value interact.
Age	≥70 years	40.8 (7.2)	53.4 (7.1)	0.38
	<70 years	26.5 (6.3)	27.3 (6.4)	
Gender	Male	34.9 (5.3)	39.9 (5.3)	0.77
	Female	24.1 (10.8)	34.2 (11.2)	
NYHA	Class II	22.8 (6.7)	26.9 (6.7)	0.75
	Class III	42.6 (6.7)	51.1 (6.7)	
LVEF	LVEF ≥27%	21.3 (6.6)	35.2 (6.6)	0.23
	LVEF <27%	44.9 (6.8)	42.7 (6.8)	
Prior HF decompensation	Yes	30.1 (5.2)	44.5 (5.2)	0.005
	No	47.5 (12.1)	11.0 (11.6)	
ICD + prior HF decompensation	Yes	29.4 (7.9)	54.7 (8.1)	0.04
	No	34.7 (6.0)	30.6 (5.9)	
PHQ-9 depression score <10	Yes	49.4 (10.1)	29.1 (10.2)	0.03
	No	27.8 (5.5)	42.0 (5.5)	

Mean SE

Profiling of Patients with Benefits (HF hospitalization + LVEF \geq 25% + PHQ <10)



		RTM Events	UC Events	Hazard Ratio (95% CI)	P within group	P interaction
CV mortality						
HF Hospitalization + LVEF \geq 25 % + PHQ<10	Yes 333 (47%)	12	25	0.48 (0.24-0.95)	0.035	0.024
	No 387 (53%)	28	21	1.32 (0.75-2.32)	0.34	

		Days	Days		P within group	P interaction
Days lost due to death or HF hospitalization						
HF Hospitalization + LVEF \geq 25 % + PHQ<10	Yes 333 (47%)	22.0 (7.0)	43.5 (6.9)		0.03	0.03
	No 387 (53%)	42.0 (6.5)	34.6 (6.6)		0.42	

Conclusions

- **In stable ambulatory heart failure patients with guideline based therapy, remote telemedical management does not reduce a low All-cause Mortality**
- **Important aspects of quality of life (i.e. physical functioning) can be improved by remote telemedical management.**
- **Subgroup with possible benefit that requires further investigation:**
 - HF patients with prior HF hospitalization
 - HF patients without depression
 - HF patients without very low LVEF (i. e. <25%)
- **Implications for clinical practice:**
 - Telemedicine is not for all HF patients
 - Telemedicine for unstable HF patients could be a “Bridge to Stability“
 - Need for further trials in defined patient subgroups
 - Development of specific methodology for randomized telemedical trials

Thank you / Disclosure



Thanks to the
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Disclosure Prof. Koehler

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