Telemedicine to reduce mortality in ambulatory patients with heart failure – Lessons from the TIM-HF2 trial

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Declaration of interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company (Abbott (Honoraria for advisory board activities))
- Research contracts (Research Grant of the German Federal Ministry Education and Research: TIM-HF2)
- Others (Cochlear AG; Boston Scientific (both Honoraria for lectures))

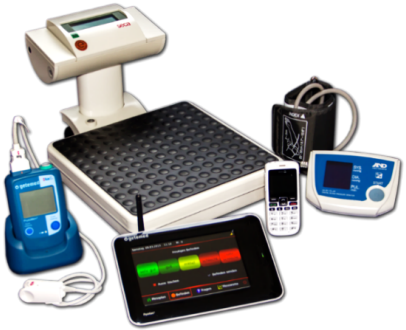
Questions

- Do you think, telemedicine will become a routine in heart failure (HF) care for selected patients outside clinical trials?
- Do you think, telemedicine is an opportunity to overcome regional differences in HF care?
- Do you think, Telemedical Centres will be the upcoming structure to provide telemedicine in HF care?
- Do you think, implants or m-health will be the primary technology to obtain vital parameters on a daily basis?
- Do you think, artificial intelligence (AI) could have a role in HF care (“Autopilot” for HF)?

Concept of Remote Patient Management

Remote Patient Management (RPM)

- Telemonitoring
- Education + Self-Empowerment
- Guideline-based HF therapy



Anker SD/ Koehler F et al. Lancet. 2011 Aug 20;378(9792):731-9.

Role of Telemedical Centres

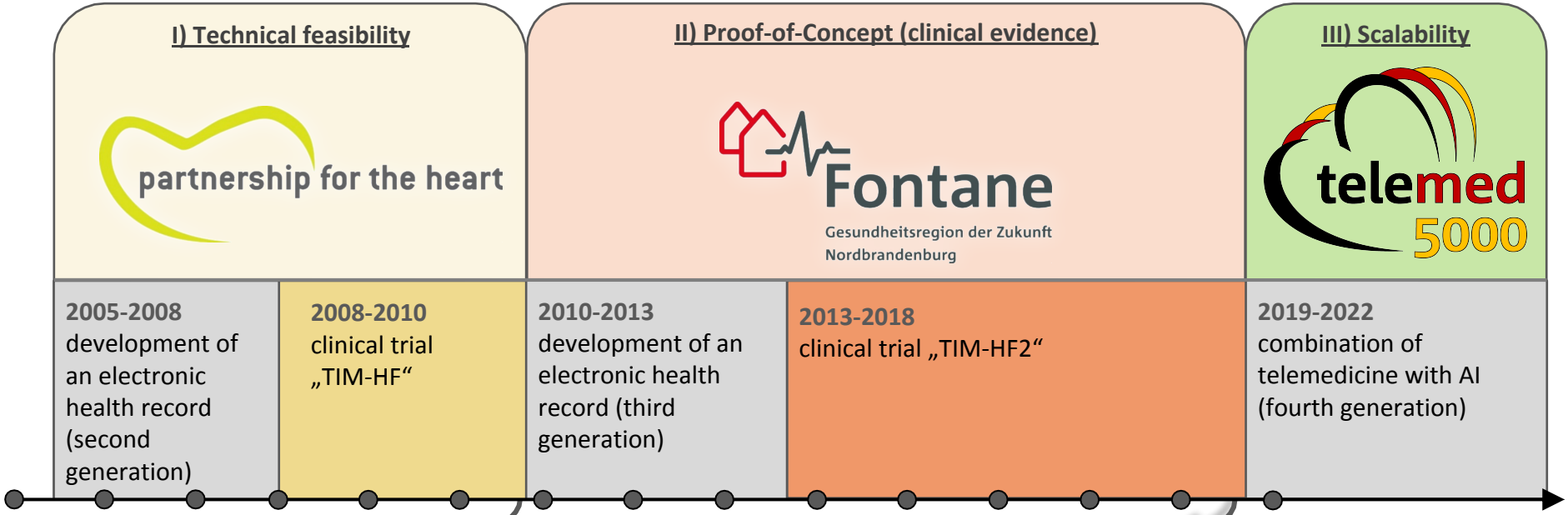
General Requirements

- Division of the Department of Cardiology
- Led by HF specialists (Cardiologists and HF Nurses)
- 24/7 RPM

Networks between Telemedical Centres (TMC) of 1 and 2 levels:

1st Level Telemedical Centre	2nd Level Telemedical Centre
• Working hours: 8 am to 5 pm • Workload: 200 patients	• Working hours: 24/7 • Workload: 500 patients during daytime + additonal patients from 1st level TMC´s during night time (approx. 1.000 patients)

Telemedical Interventional Management in HF: Study program



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Circulation
An American Heart Association Journal

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

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THE LANCET

Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial

Supported by:

Federal Ministry for Economic Affairs and Energy

on the basis of a decision by the German Bundestag

TIM-HF2: Trial Objectives

TIM-HF2 was designed

- to investigate the impact of RPM on mortality, morbidity and Quality of Life focusing on a HF population recently hospitalised for worsening HF and who do not have major depression.
- to determine if regional differences in HF care – i.e. rural versus metropolitan area – have impact on outcome.
- to investigate if the benefits seen on morbidity and mortality for the RPM group during the 12-month follow-up in the main TIM-HF2 trial would be sustained over the subsequent 12 months after stopping the RPM intervention (extended follow-up period).

TIM-HF2: Study Design

Study type/patient characteristics: multicentre RCT in Germany, 1538 HF patients, hospitalised for HF maximally 12 months previously, with no major depression (PHQ-9<10) and with a LVEF ≤45% or if >45%, diuretics mandatory; 12-month follow-up under intervention

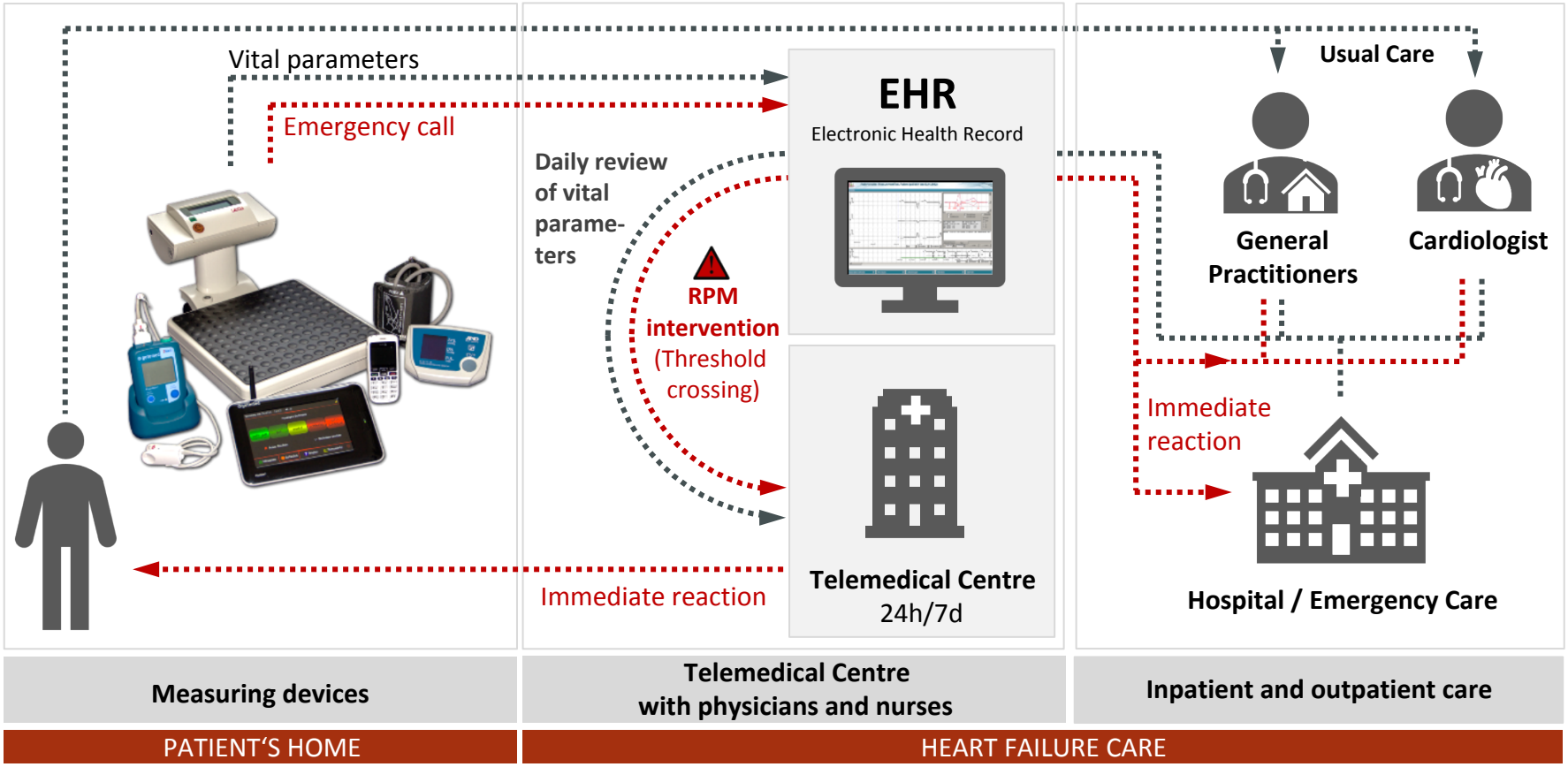
Primary Endpoint: % days lost due to unplanned CVhospital admissions and all-cause death

Secondary Endpoints: all-cause death, cardiovascular death, recurrent HF/CV-hospital admissions, health economics, biomarkers, quality of life

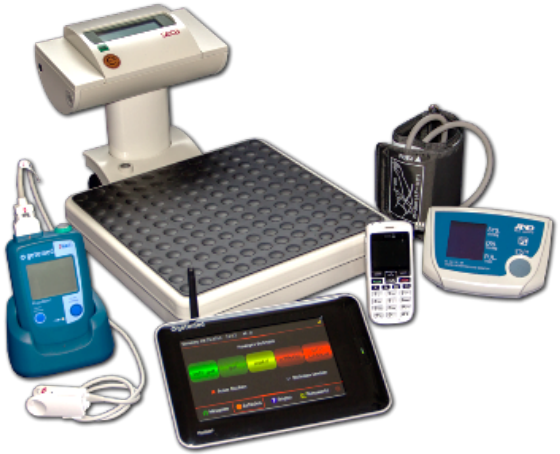
Intervention: Remote Patient Management (RPM) vs Usual Care (UC)

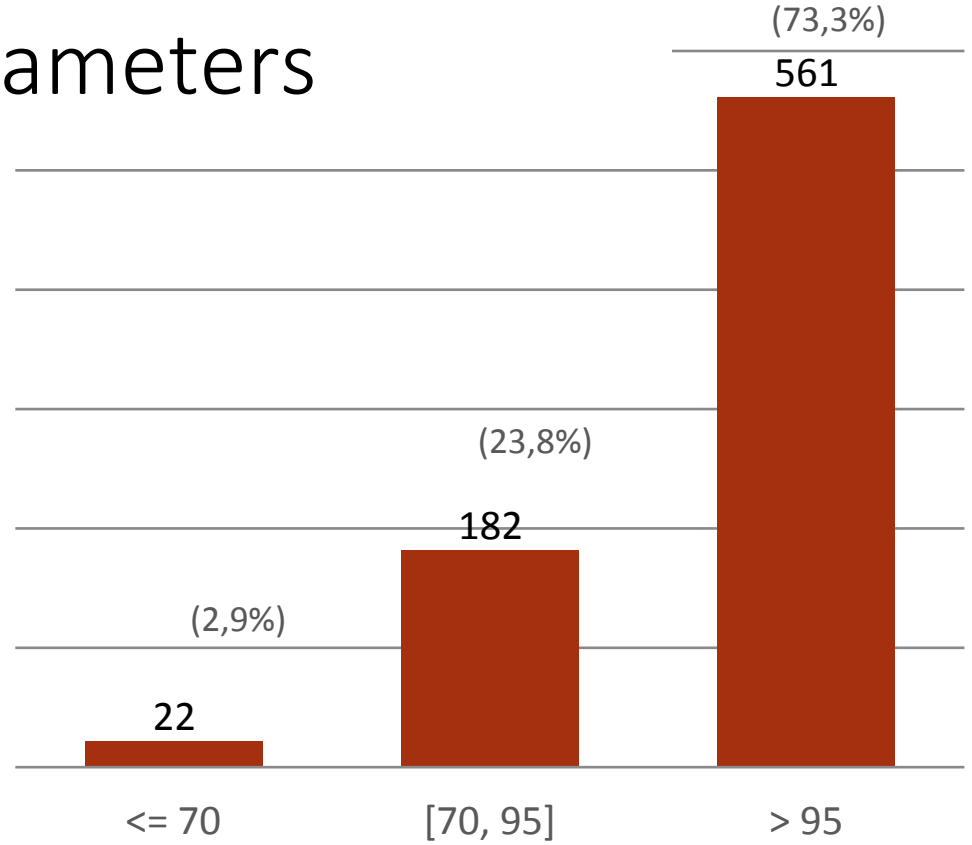
Koehler F et al. Eur J Heart Fail. 2018;20:1485-93

TIM-HF2: RPM Intervention



Adherence to the daily data transfer of vital parameters





Telemedical Interventions TIM-HF2

Intervention	Number of interventions	Average per Patient	Median per Patient	Min	Max
Evaluation of patient transmitted vital parameters*	1,026,078	1,341	1,421	6	3,962
Patient case review by TMC** physicians and nurses	38,694	50	36	0	273
Monthly structured telephone interview	9,189	12	12	1	13
TMC initiated contact with patient for evaluation of critical vital parameters	4,324	5	4	0	37
TMC initiated contact with patient after discharge, physician appointment and for validation of medication list	6,037	8	7	1	27
TMC initiated medication change(s)	3,546	5	3	0	57
TMC initiated scheduled 3-month medical report sent to patient's local physician (GP or cardiologist)	2,812	4	4	0	4
TMC physician and patient telephone consultations	1,535	2	1	0	40
TMC initiated contact with health care professionals	863	1	1	0	21
Patient home HF education including caregivers	765	1	1	1	1
TMC initiated emergency department visits	30				
TMC initiated unplanned cardiovascular hospitalisations	57				
TMC initiated unplanned non-cardiovascular hospitalisations	13				

*Vital parameters= body weight, blood pressure, self-rated health status, ECG incl. SpO2

**TMC, Centre for Cardiovascular Telemedicine

Koehler F et al. Lancet. 2018 Sep 22;392(10152):1047-57

Primary Outcome

% days lost due to unplanned CV hospitalisations and all-cause death

	RPM (n=765)		Usual Care (n=773)			
	# Patients with event (%)	Weighted Average of Percentages (95% CI)	# Patients with event (%)	Weighted average of percentages (95% CI)	Ratio RPM vs. UC (95% CI)	P
% days lost due to unplanned CV hosp. and all-cause death	265 (35)	4.88 (4.55, 5.23)	290 (38)	6.64 (6.19, 7.13)	**0.804 (0.65, 0.99)**	**0.046**
Days lost (days/year)		17.8 (16.6, 19.1)		24.2 (22.6, 26.0)		

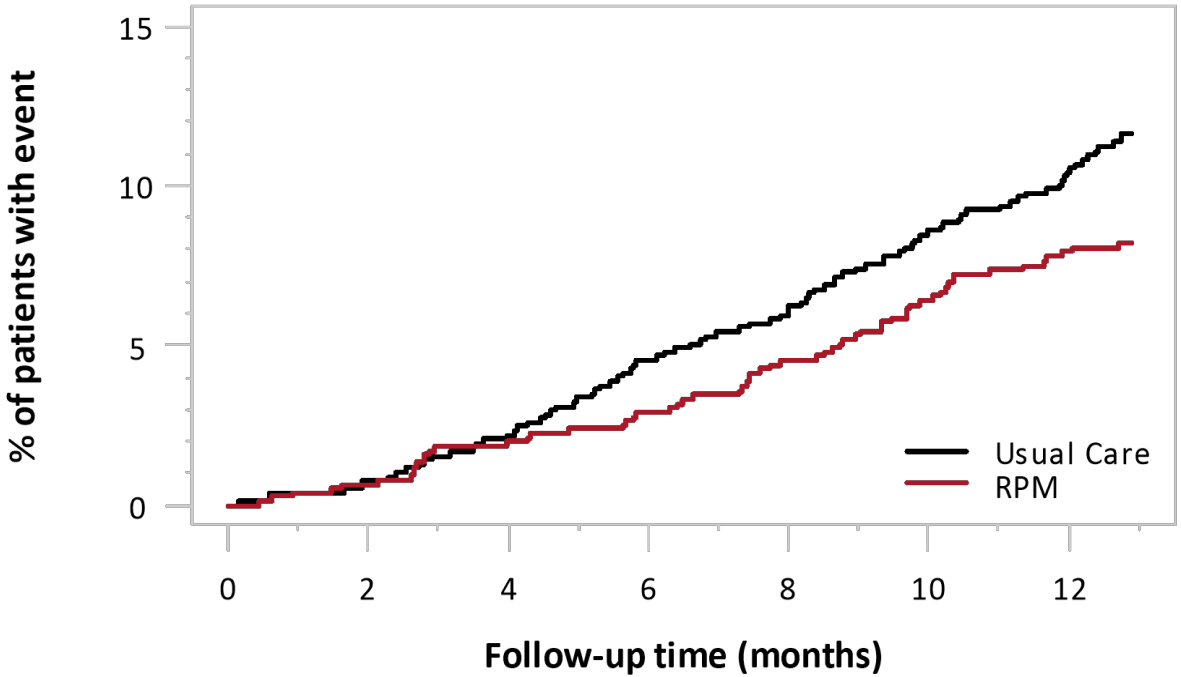
Koehler F et al. Lancet. 2018 Sep 22;392(10152):1047-1057

Secondary Outcomes (1): All-cause mortality

HR 0.70

95% CI 0.50, 0.96

P=0.028



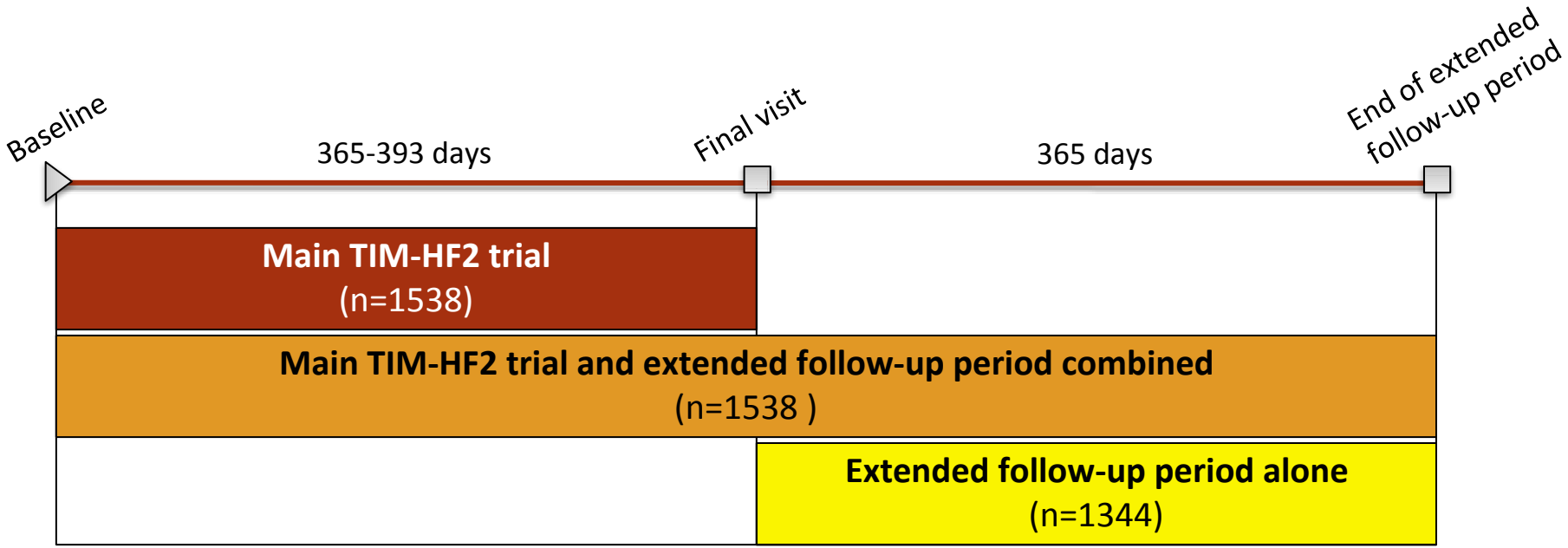
No. At Risk							
Usual Care	773	767	756	738	716	697	681
RPM	765	755	737	724	709	688	673

Secondary Outcomes (II): Recurrent HF hospital admissions

	RPM (n=765, 739.6 patient years)			UC (n=773, 754.4 patient years)				
	No. of patients with HF hosp. (%)	No. of HF hosp.	Incidence (95% CI)	No. of patients with HF hosp. (%)	No. of HF hosp.	Incidence (95% CI)	Ratio RPM vs. UC (95% CI)	p
HF hospital admissions and all-cause death	164 (21)	280	0.441 (0.369–0.528)	223 (29)	405	0.653 (0.553–0.771)	**0.676** (0.529–0.862)	**0.0016**
HF hospital admissions and CV death	153 (20)	265	0.414 (0.345–0.498)	210 (27)	379	0.596 (0.502–0.707)	**0.696** (0.541–0.894)	**0.0047**

IRR=Incidence rate ratio; incidence = events/100 patient years of follow-up; CV=cardiovascular; HF=heart failure; hosp.=hospital admissions

Definition of the follow-up periods



Primary Outcome (I)

Main TIM-HF2 trial and extended follow-up period combined

	RPM (n=765)		UC (n=773)			
	No. of patients with event (%)	Weighted average of percentages (95% CI)	No. of patients with event (%)	Weighted average of percentages (95% CI)	Ratio RPM vs. UC (95% CI)	p
% days lost due to unplanned CV hosp. and all-cause death	382 (50%)	9.28% (7.76–10.81)	398 (51%)	11.78% (10.08–13.49)	0.79 (0.62–1.00)	**0.0486**
Days lost		67.7 days (56.6–78.9)		86.0 days (73.6–98.5)		

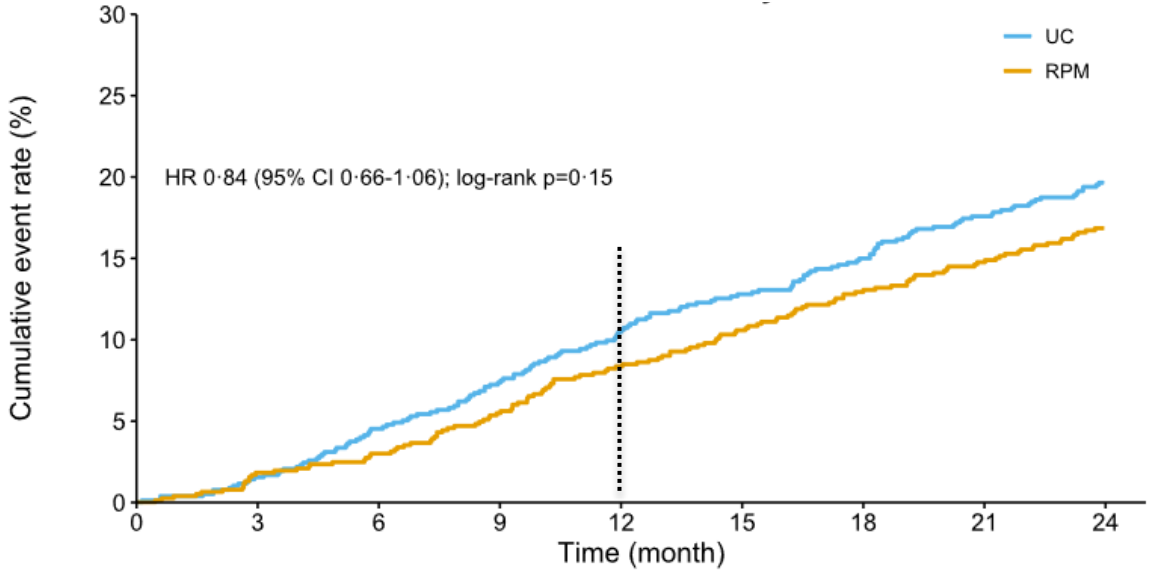
Extended follow-up: Primary Outcome (II)

Extended follow-up period alone

	RPM (n=671)		UC (n=673)			
	No. of patients with event (%)	Weighted average of percentages (95% CI)	No. of patients with event (%)	Weighted average of percentages (95% CI)	Ratio RPM vs. UC (95% CI)	p
% days lost due to unplanned CV hosp. and all-cause death	198 (30%)	5.95% (4.59–7.31)	194 (29%)	6.64% (5.19–8.08)	0.97 (0.78–1.21)	**0.82**
Days lost (days/year)		21.7 days (16.7–26.7)		24.2 days (19.0–29.5)		

All-cause death (I)

Main TIM-HF2 trial and extended follow-up period combined

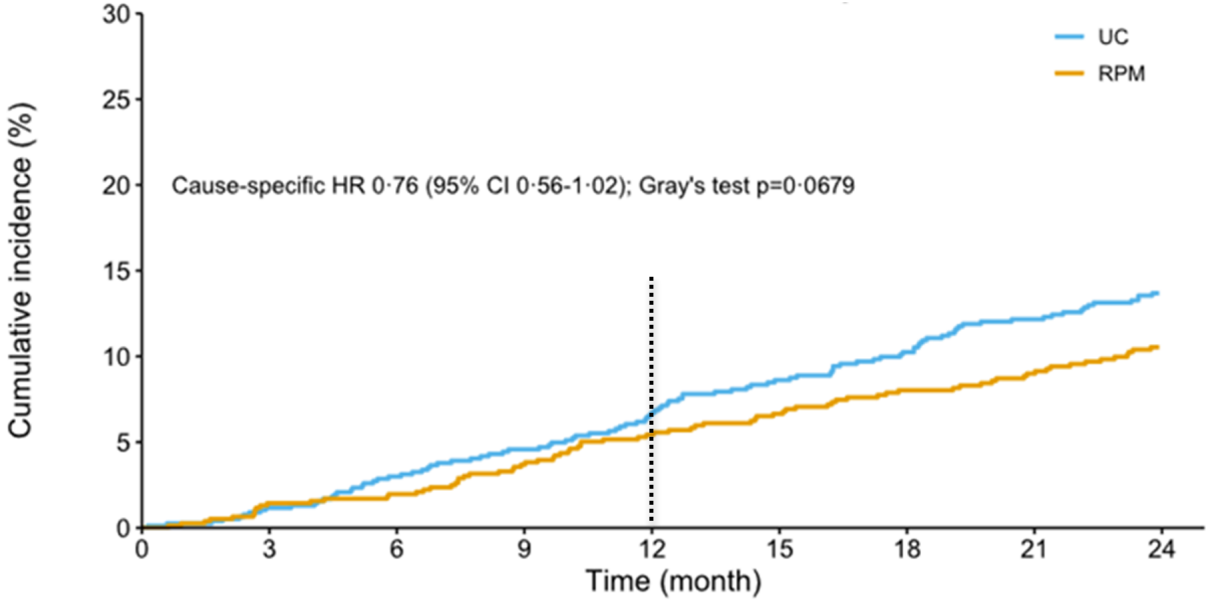


Number at risk

UC	773	761	738	716	692	674	657	637	621
RPM	765	751	742	723	701	684	666	652	636

Cardiovascular death

Main TIM-HF2 trial and extended follow-up period combined



Number at risk

UC	773	761	738	716	692	674	657	637	621
RPM	765	751	742	723	701	684	666	652	636

Aalen-Johansen cumulative incidence

Conclusion

1. Remote Patient Management (RPM) is a complex care intervention „add-on“ to guideline-based therapy of GPs, HF-nurses and specialists.

2. RPM will be a part of a holistic HF-care for specific cardiological patients.

3. The positive impact of RPM on morbidity persisted up to one year after stopping the RPM intervention, but in an attenuated manner.

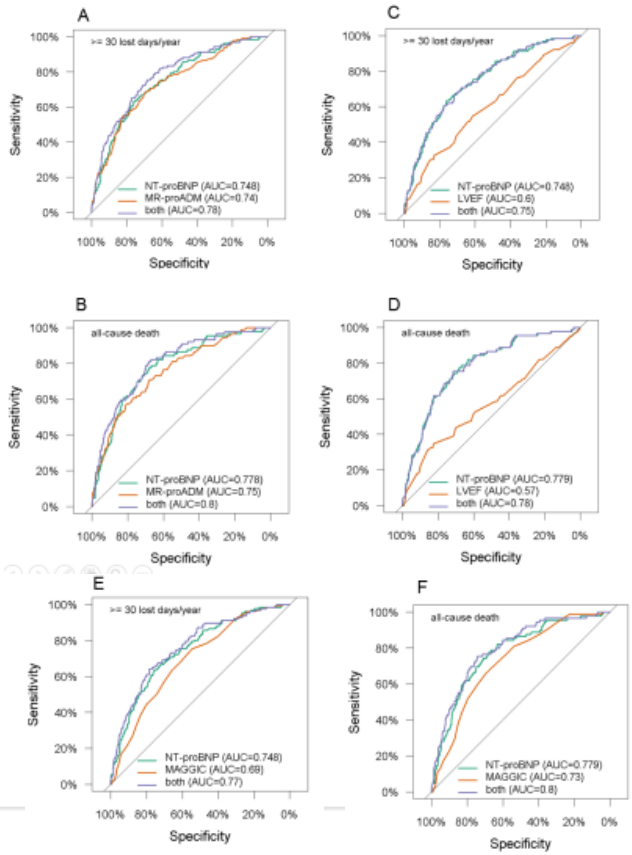
4. All-cause (& CV) mortality were similar between groups after stopping RPM.

5. The results of TIM-HF2 Extended follow-up suggest that the RPM intervention is only effective, if the RPM intervention is ‘turned on’.

Backup

Biomarker guidance to start RPM

- Biomarkers NT-proBNP and MR-proADM have strong associations with outcome.
- Biomarkers allow identification of patients recommended for RPM with 95% sensitivity, in the most efficient scenario (excluding 27% of patients; NT-proBNP<413.7pg/ml and MR -proADM<0.75nmol/L)
- Number-needed-to-treat (NNT) for all-cause death was lowered from 28 to 21
- Rate of emergencies and telemedical efforts were significantly lower among patients not recommended for RPM
- Biomarker guidance would save about 150 hours effort/year per 100 eligible patients



Möckel M et al. Eur J Heart Fail. 2019 May 25.

TIM-HF2: Patient Profile

Inclusion Criteria

- Diagnosed with HF – NYHA class II or III
- HF hospitalisation within maximally 12 months prior to randomisation
- Depression score PHQ-9 <10
- LVEF ≤45% or LVEF >45% + oral diuretics
- Written informed consent

Main Exclusion Criteria

- Hospitalisation 7 days before randomisation
- Implanted cardiac assist system
- ACS ≤7 days before randomisation
- Urgent status for heart transplantation
- Planned revascularisation, TAVI, MitraClip and/or CRT-implantation within 3 months after randomisation
- Revascularisation and/or CRT-implantation ≤28 days before randomisation
- Terminal renal insufficiency with hemodialysis
- Life expectancy < 1 year

Koehler F et al. Eur J Heart Fail. 2018 Oct;20(10):1485-93