Which telemonitoring strategy provides clinical benefits?

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Expert Meeting Berlin
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Epidemiology for Heart Failure Remote Patient Management

Epidemiology

- Incidence approx. 2.5 million patients
  (every tenth German citizen over 65 years)
- Approx. 200,000 new cases per year
- Approx. 11 % Mortality in class NYHA II/III per year

Morbidity

- **Major cause of hospitalization**
- **Non-cardiovascular co-morbidity** (e.g. renal failure, COPD; depression)
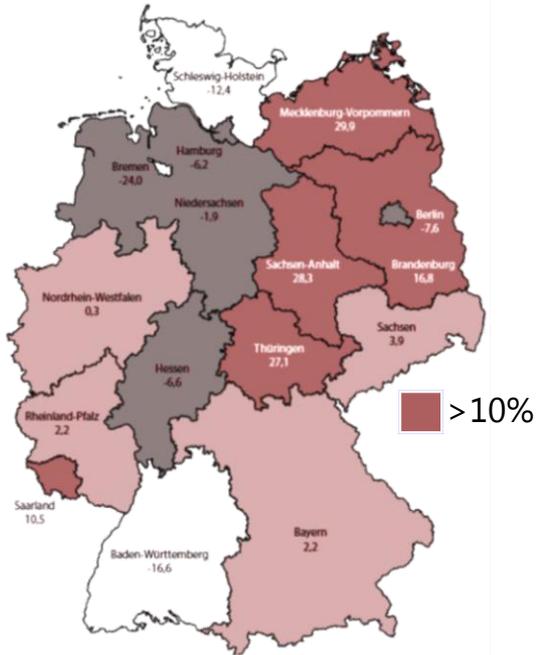- **200,000 patients with >450,000 HF-hospitalizations** p.a.

Need for RPM

- **100,000 patients** in class NYHA II/III and without obstructing co-morbidities (e.g. dementia)
- Number of patients in clinical trials: 1,000-1,500

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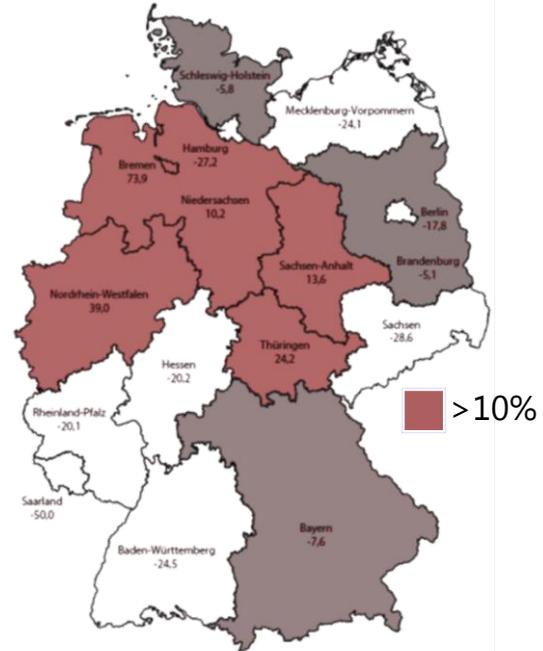
Regional Differences in HF patient care

HF morbidity
Deviation from national average

HF mortality
Deviation from national average

Rationale of e-Health at Home for HF-Management
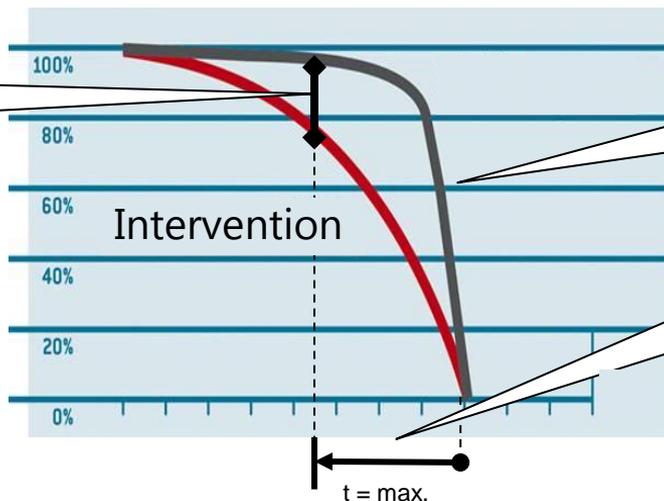
Concept of Remote Patient Management

Remote Patient Management

Telemonitoring

Education + Self-Empowerment

Guideline-based HF-therapy

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

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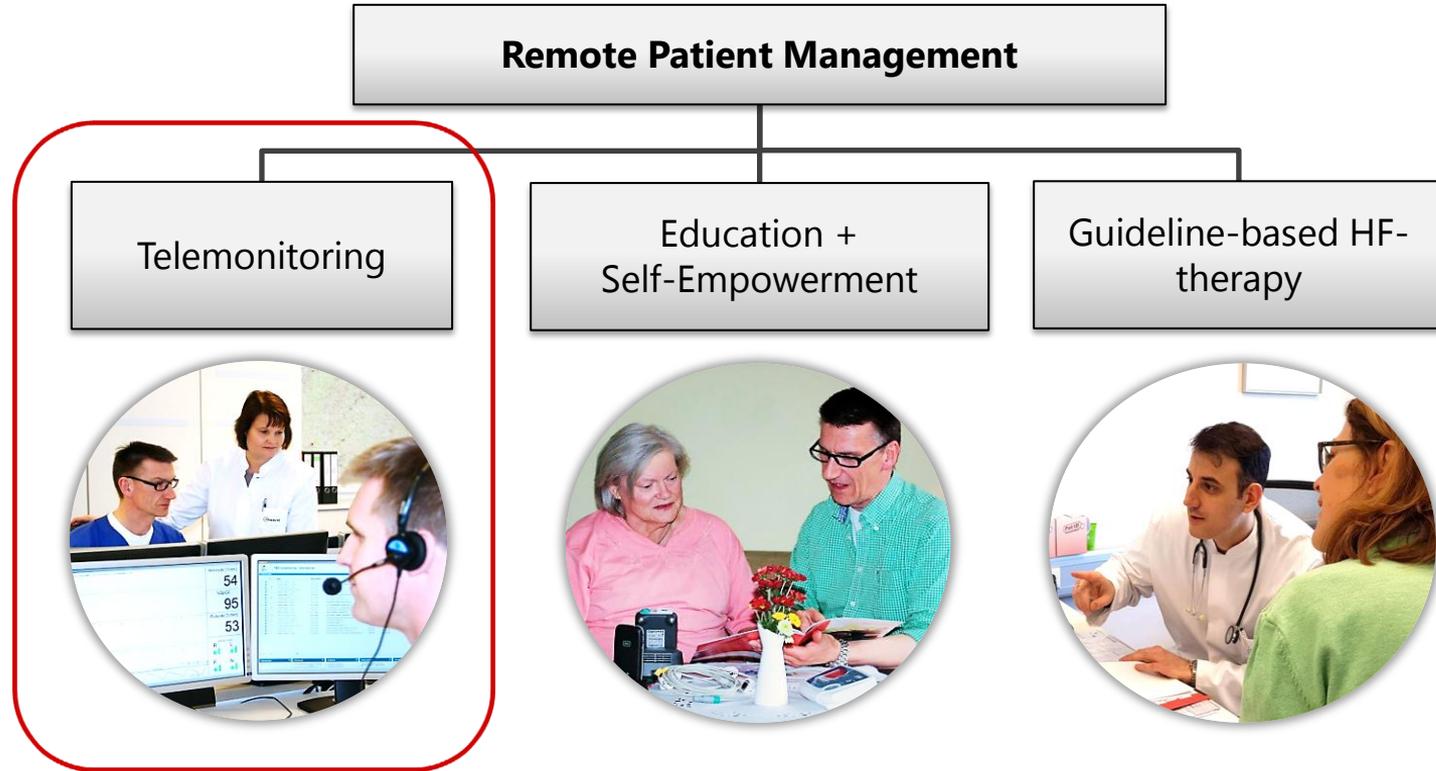
Telemonitoring as an Element of Remote Patient Management

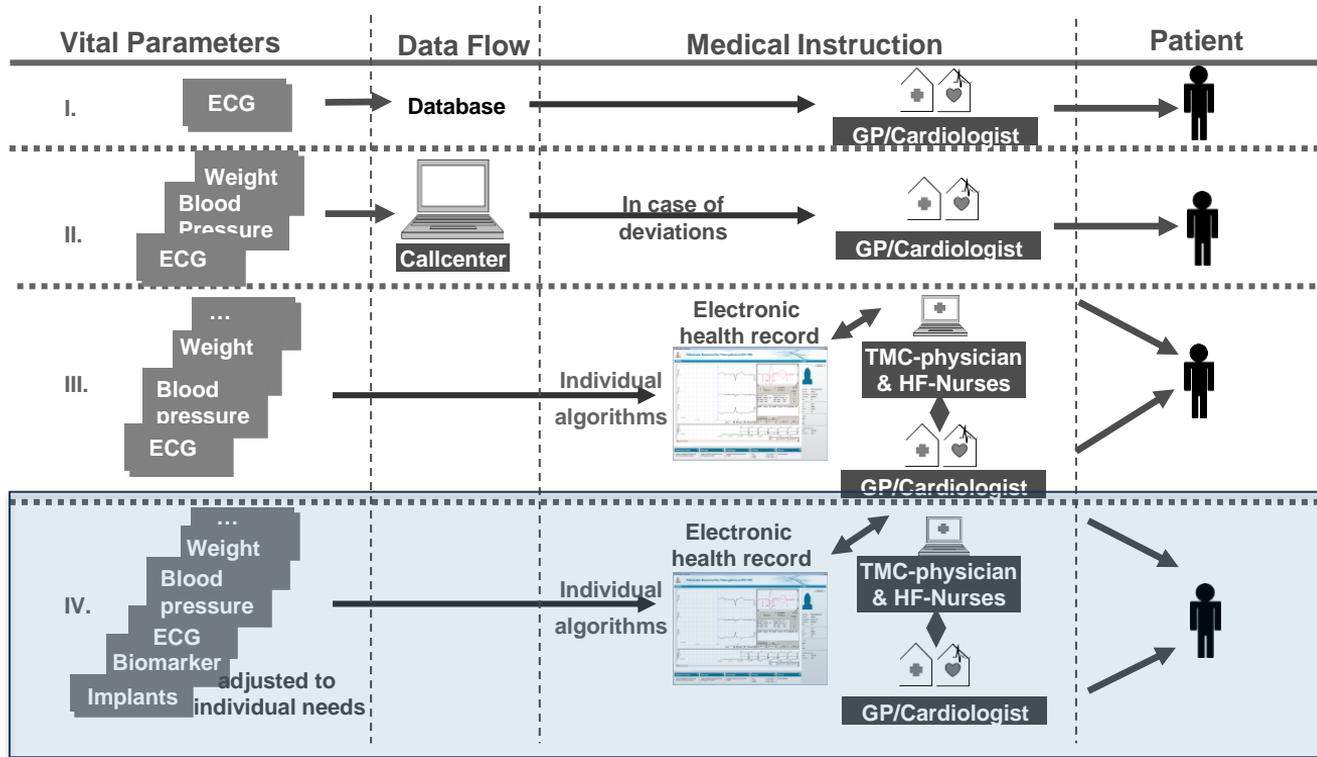| Non-invasive measurement of vital parameter | Biomarker measurement at home | Monitoring using implantable devices | Smartphones |

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Four Generations of Telemonitoring Systems

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

RCTs for Telemedicine in HF

RPM with Telephone Support/ Education

INH-Study	*(Circ Heart Fail 2012)*	715 Patients, Germany

RPM with noninvasive Telemedicine

TIM-HF2	***(Lancet 2018)***	**1,538 Patients, German**y
TIM-HF	*(Circulation 2011)*	710 Patients, Germany
CardioBBEAT	*(Trials 2015; ACC 2017)*	621 Patients, Germany
BEAT-HF	*(JAMA 2016)*	1,437 Patients, USA

RPM with invasive Telemedicine (Implants)

REM-HF	*(Eur Heart J 2017)*	1,650 Patients, United Kingdom
IN-TIME	***(Lancet 2014)***	**716 Patients, Germany**
CHAMPION-Trial	***(Lancet 2011, 2016)***	**550 Patients, USA**
OptiLINK-HF	*(Eur Heart J 2016)*	1,002 Patients, Germany

IN-TIME Trial

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*

Study design: RCT, prospective, multicentre, n=716, heart failure patients with reduced EF (≤35%), implanted ICD or CRT-D, 1:1 randomisation 1 month after hospital discharge, follow-up: 12 months, NCT00538356

Primary Endpoint: Composite score of death, hospitalisation due to heart failure, NYHA class and global assessment score (Packer-Score)

Secondary Endpoints: Total mortality and rehospitalisations due to progressive heart failure, correlation of Home Monitoring values with the clinical status, incidence and reasons for Home Monitoring based interventions, Home Monitoring workflow analysis

Intervention: ICD or CRT-D with activated Home Monitoring feature (BIOTRONIK Home Monitoring®)

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IN-TIME Trial: Results

All-cause mortality was reduced by > 50%
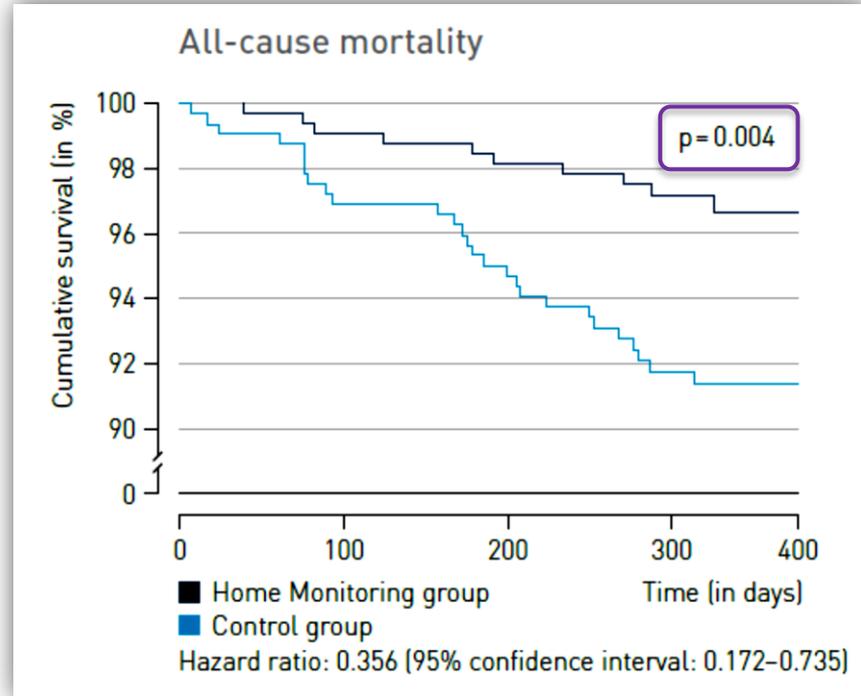
CHAMPION* Trial

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*

Summary

Background Results of previous studies support the hypothesis that implantable haemodynamic monitoring systems might reduce rates of hospitalisation in patients with heart failure. We undertook a single-blind trial to assess this approach.

*CardioMEMS Heart Sensor Allows Monitoring of Pressures to Improve Outcomes in NYHA Functional Class III Heart Failure Patients

Study design: RCT (1:1), NYHA III patients hospitalized for heart failure within the past 12 months; n=570; multicentre (n=64); single-blinded; follow-up: mean 15 month (at least: 6 months); (NCT00531661)
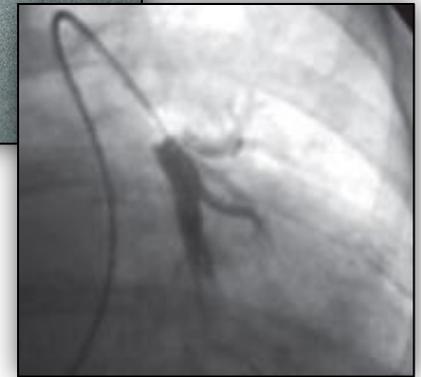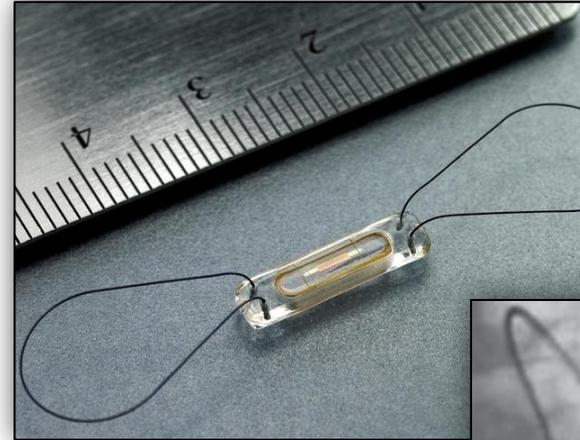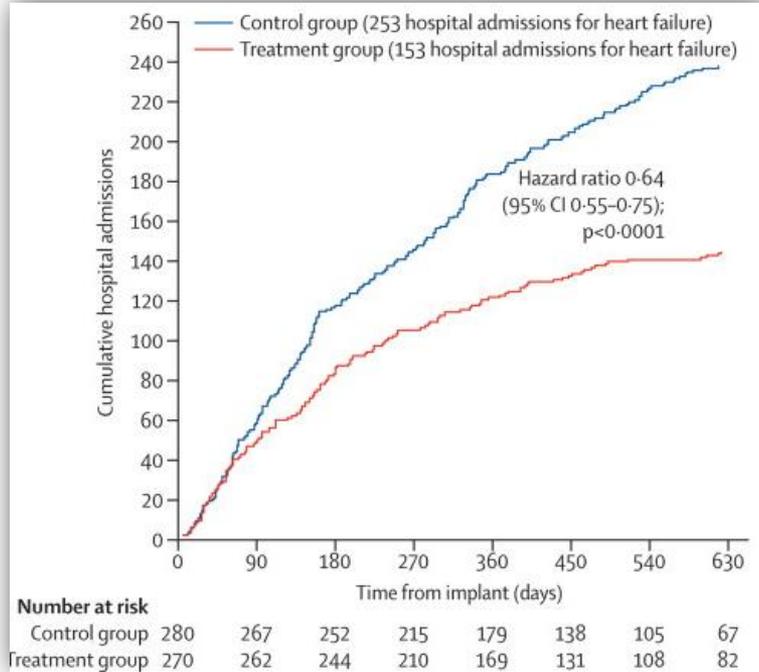
Primary Endpoint: Rate of HF-hospitalization

Secondary Endpoints: Device-related complications, change in pulmonary pressure up to 6 months (relative to baseline)

Intervention: Drug changes based on standard care and daily transferred   sensor hemodynamics ($2^{nd}/3^{rd}$ Generation)

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"Rate of HF-related Hospitalisations"

THE LANCET

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

Friedrich Koehler, Kerstin Koehler, Oliver Deckwart, Sandra Prescher, Karl Wegscheider, Bridget-Anne Kirwan, Sebastian Winkler, Eik Vettorazzi, Leonhard Bruch, Michael Oeff, Christian Zugck, Gesine Doerr, Herbert Naegele, Stefan Störk, Christian Butter, Udo Sechtem, Christiane Angermann, Guntram Gola, Roland Prondzinsky, Frank Edelmann, Sebastian Spethmann, Sebastian M Schellong, P Christian Schulze, Johann Bauersachs, Brunhilde Wellge, Christoph Schoebel, Milos Tajsic, Henryk Dreger, Stefan D Anker*, Karl Stangl*

TIM-HF2: Trial Objectives

The "Telemedical Interventional Management in Heart Failure II" (TIM-HF2) trial 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.

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TIM-HF2: Study Design and Study Flow

- Prospective, randomised (1:1), controlled, open, parallel-group, multi-centre trial

- Recruitment: **1538 patients** recruited between Aug 2013 and May 2017 (765 RPM, 773 Usual Care)

| **Screening Visit**
done by GP or Cardiologist | → | **Baseline Visit**
done by Cardiologist;
Randomisation | → | **RPM Group**
Daily data transfers to the TMC

Usual Care Group | → | **3 month visit**
done by GP or Cardiologist | → | **6 month visit**
done by GP or Cardiologist | → | **9 month visit**
done by GP or Cardiologist | → | **12 month final visit**
done by Cardiologist |
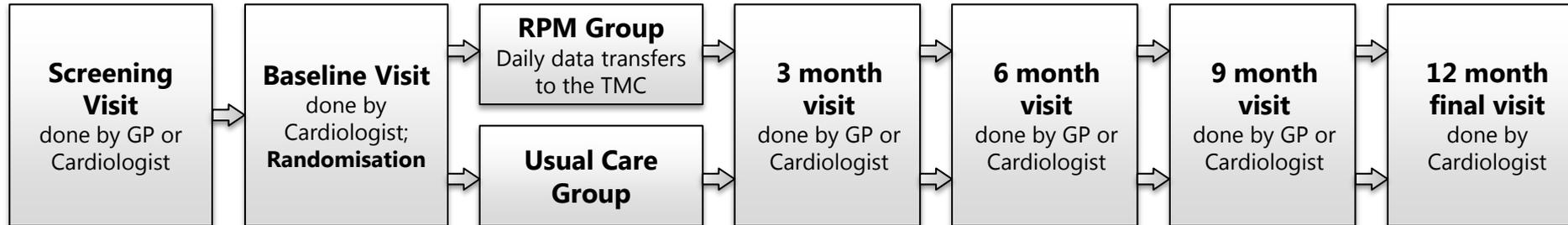
TIM-HF2: Participating Sites

- **113 Cardiology sites**
  - 43 Regional / local hospitals
  - 10 University hospitals
  - 60 Cardiology outpatient practices
- **87 General practitioners**

Sites were located in 14 metropolitan areas and 11 rural areas within 13 of 16 German states.
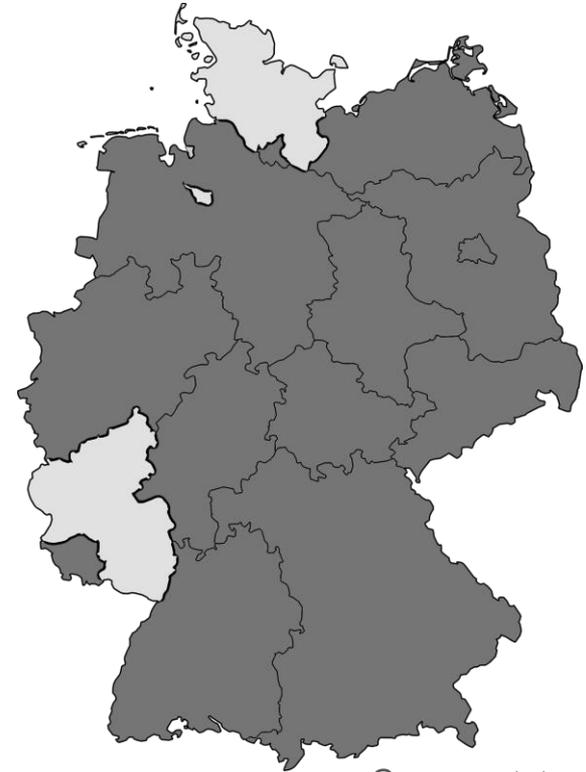
German states

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

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TIM-HF2: RPM Intervention
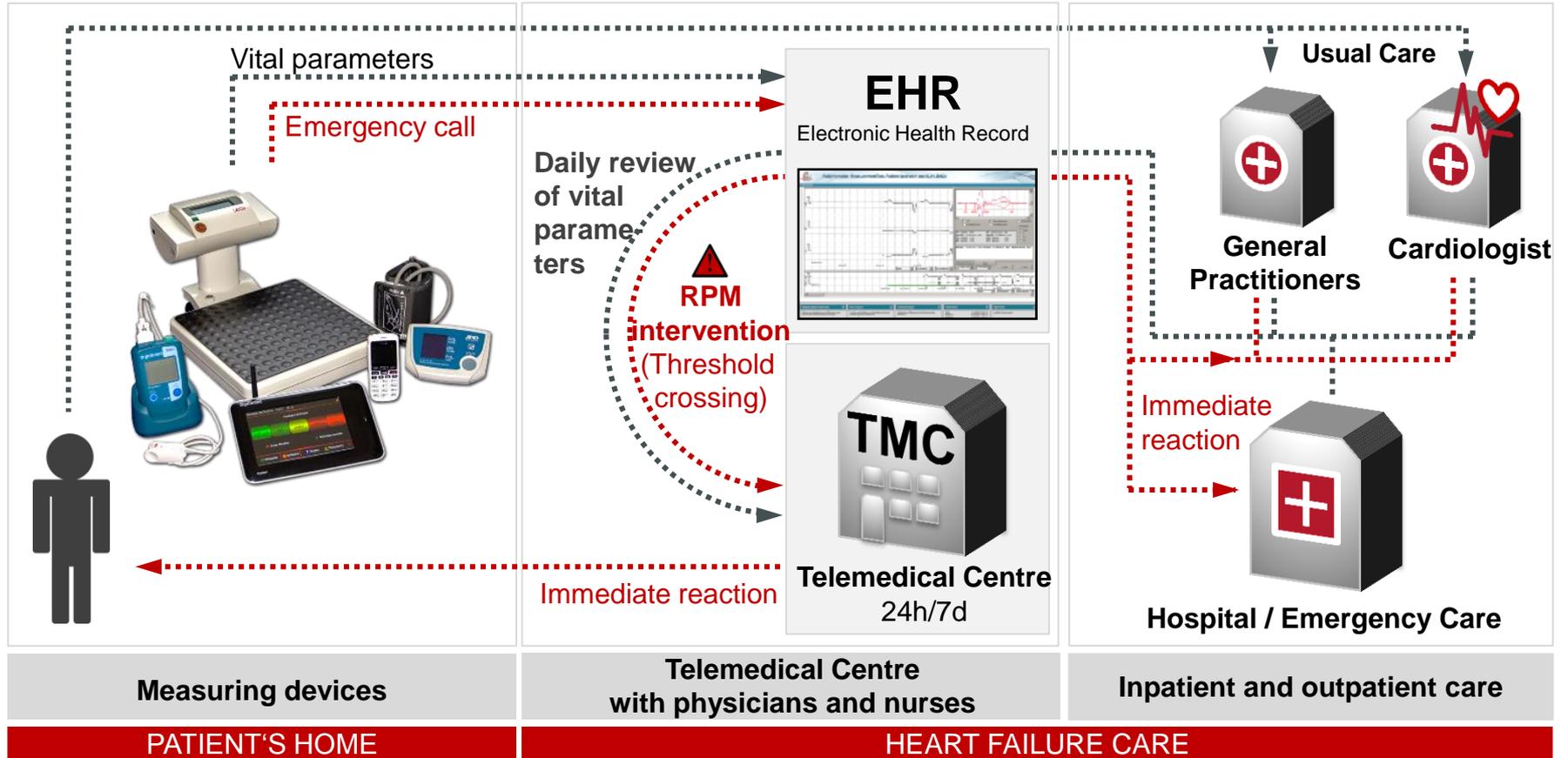
Primary Outcome

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

	RPM (n=765)		Usual Care (n=773)		Ratio RPM vs. UC (95% CI)	P
	# Patients with event (%)	Weighted Average of Percentages (95% CI)	# Patients with event (%)	Weighted average of percentages (95% CI)		
% 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)		

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Main Secondary Outcome

% days lost due to unplanned HF hospitalisations

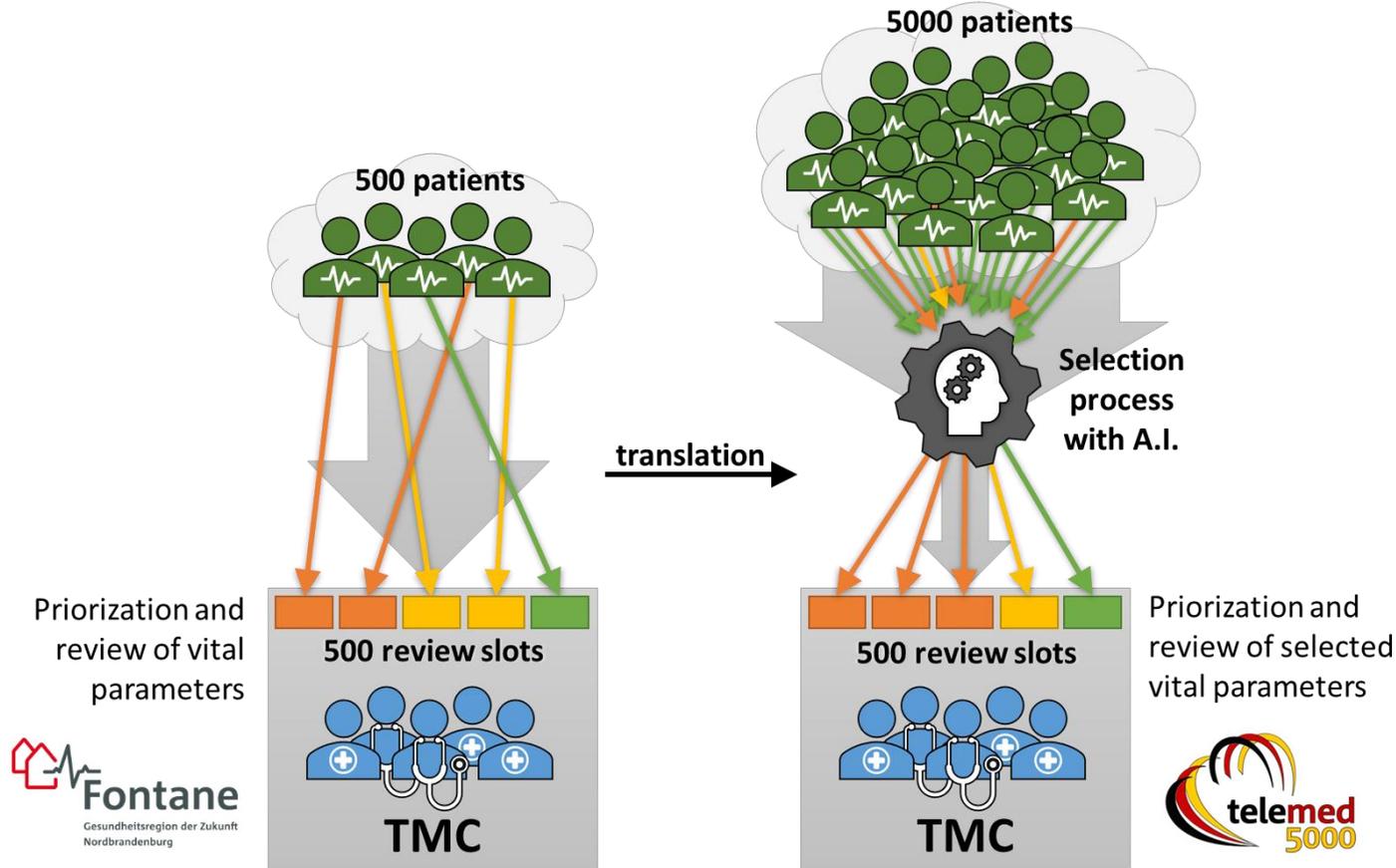|	RPM (n=765)		Usual Care (n=773)		Ratio RPM vs. UC (95% CI)	P
	# Patients with event (%)	Weighted Average of Percentages (95% CI)	# Patients with event (%)	Weighted average of percentages (95% CI)		
% days lost due to unplanned HF hospitalisations	140 (18)	1.04 (0.96, 1.11)	193 (25)	1.53 (1.43, 1.64)	0.797 (0.67, 0.95)	0.007
Days lost (days/year)		3.8 (3.5, 4.1)		5.6 (5.2, 6.0)		

Selected Subgroups – unplanned CV hosp. and all-cause mortality

Subgroup	No. of Patients (%)	RPM	UC	Effect (95% CI)		P Value for Interaction
		Weighted Average of Percentages				
All patients	**1538**	**4.80**	**6.60**	**0.80 (0.65, 1.00)**		
Region						0.658
Rural	915 (59)	4.76	6.35	0.82 (0.62, 1.11)		
Urban	623 (41)	5.96	7.05	0.78 (0.56, 1.08)		
Gender						0.154
Female	468 (30)	4.03	4.67	0.62 (0.26, 1.45)		
Male	1070 (70)	5.24	7.50	0.72 (0.56, 0.95)		
Age						0.883
≤Median 73	816 (53)	3.51	5.40	0.81 (0.60, 1.09)		
> Median 73	722 (47)	6.43	8.07	0.79 (0.57, 1.08)		
LVEF						0.156
>45	537 (35)	4.74	5.30	0.98 (0.68, 1.42)		
≤45	1001 (65)	4.96	7.33	0.73 (0.56, 0.97)		

0.25   0.5   1

Favours RPM ← → Favours Usual Care

Scaling up the number of patients per TMC:

a) Artifical Intelligence for priorization of patients at the telemedical center

b) Artifical Intellligence in new devices

Network between Telemedical Centers of 1st and 2nd level:

1st Level:
- Working hours: Mo-Fr; 9-5 h;
- Workload: ca. 200 Patients

2nd Level Telemedical Center:
- Working hours: 24/7;
- Workload: daily RPM of the own patients (500 Patients)
- During night times RPM for the own patients + RPM of the patients from different 1st level TMC´s (approx. 1.000 patients)

Actors involved in HF-discharge-management:

- General Practitioner
- HF-Nurse
- Outpatient clinic
- Hospital
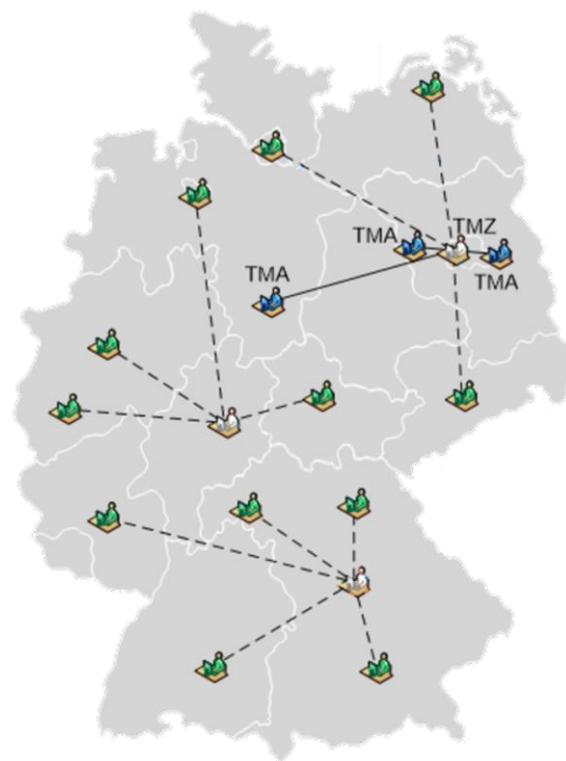
Conclusion

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. Current proof of benefits is only for HF-patients in functional class NYHA II/III after hospitalization due to hydropic decompensation

4. RPM is an effective approach to overcome regional differences in HF management (TIM-HF2 study)

5. Development of telemedicine technologies for HF-Patients includes the sensor technologies and the whole system of data transfer

6. regional TMC´s as a key element in RPM)