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Disease manifestation and disease management in chronic heart failure

Submission date	Recruitment status	[_] Prospectively registered
21/09/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/11/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/01/2021	Circulatory System	

Plain English summary of protocol

Background and study aims
Heart failure is frequent, increasing in prevalence, and is associated with high morbidity, mortality and costs. In order to reduce morbidity (illness) and mortality (death rate) in high-risk patients who have already experienced an episode of acute cardiac decompensation, appropriate comprehensive monitoring and collaborative treatment are of key importance. Unlike in other chronic diseases (e.g. diabetes mellitus) there is limited availability of comprehensive heart failure disease management within the German Health Care System, and targeted interventions considering patients individual risk profiles and their changes over time are lacking. This study compares a structured nurse-coordinated collaborative disease management intervention with usual care. HeartNet-Care-HF™ was developed in Germany for post-inpatient care and includes as modules monitoring, information, self-empowerment, improvement of compliance with pharmacotherapy, suitable discharge management and networking amongst a patients different health care providers.

Who can participate?
Patients hospitalized with decompensated systolic heart failure are eligible, if aged ≥18 years and able to participate in a telephone-based intervention.

What does the study involve?
Patients will be randomly allocated to one of the two study groups: HeartNet-Care-HF™ or usual care. Patients undergoing usual care receive standard post-discharge management, which typically includes a discharge letter with recommendations for increasing the dose (up-titration) of heart failure drugs and lifestyle modifications, and an appointment with a general practitioner or cardiologist within 14 days of discharge from hospital. While still hospitalized, patients undergoing HeartNet-Care-HF™ are, in addition, trained by a specialized nurse in self-control of blood pressure, heart rate and rhythm, body weight and recognition of worsening heart failure. Nurses also ascertain that patients have body scales and blood pressure gauges at home, dispense written information on heart failure drugs and materials supporting documentation of self-monitoring results, and plan subsequent telephone-based monitoring with the patients (weekly in the first month post discharge, then according to NYHA class and

patients needs). Up-titration of guideline-recommended heart failure medication is an explicit goal of the intervention and pursued in collaboration with the patients general practitioner and /or cardiologist.

What are the possible benefits and risks of participation?
There are no risks or disadvantages of participating in the usual care group of the study, which offers heart failure treatment according to current standards. Patients in the HeartNet-Care-HF™ group receive holistic collaborative care and monitoring. The hypothesis of the study is that this treatment will improve clinical end-points as the long-term risk of mortality and re-hospitalization, reduce heart failure symptoms and lead to better quality of life. However, these hypotheses are not yet proven, and patients will have to comply with the study protocol in HeartNet-Care-HF™, which involves regular communication with the nurse and self-supervision. In summary, participation in the HeartNet-Care-HF™ group is associated with no risks, but a potential long-term benefit at the expense of some time.

Where is the study run from?
The study is coordinated by Profs. C. E. Angermann, G. Ertl and Prof. S. Störk at the Comprehensive Heart Failure Center (CHFC) at the University Hospital in Würzburg, Germany. In addition to two departments of the University Hospital, seven regional non-academic hospitals enrolled patients into the study.

When is the study starting and how long is it expected to run for?
The study started in March 2004, recruitment lasted 4 years, the study treatment was terminated after 18 months participation of each individual patient, and follow-up will continue until December 2019.

Who is funding the study?
The study is funded by the Federal Ministry of Education and Research (Germany) as part of the Competence Network Heart Failure, the Comprehensive Heart Failure Center Würzburg and by the Central Association of German Health Insurance Companies.

Who is the main contact?
Prof. Dr. med. C. Angermann
Prof. Dr. med. S. Störk

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
A standardised multidisciplinary disease management programme improves mortality and morbidity in patients with systolic heart failure - the Interdisciplinary Network Heart failure (INH) Study

Acronym
INH-Study/E-INH Study

Study objectives
Current hypotheses as of 15/01/2021:
INH-Study: Network care (HeartNet-Care-HF™) when compared to usual care reduces mortality and hospitalisation (combined primary endpoint) and/or improves quality of life 6 months after randomisation.

Extended INH-Study: Network care (HeartNet-Care-HF™) when compared to usual care reduces mortality and hospitalisation (combined primary endpoint) 18 months after randomisation. Beneficial effects on the primary and secondary endpoints (e.g. quality of life) are sustainable beyond termination of the study intervention.

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Previous hypothesis:
Network care when compared to usual care reduces mortality and hospitalisation (combined primary end point) and/or improves quality of life 6 months after randomisation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/01/2004, Ethics Committee of the Faculty of Medicine, University of Würzburg (Ethik-Kommission der Medizinischen Fakultät der Universität Würzburg), ref: 130/03
Amendment 01 approved on 19/07/2007
Amendment 02 approved on 12/08/2013
Amendment 03 approved on 14/08/2014 to extend follow-up to 120 months

Study design
Two-arm parallel-group prospective randomised controlled intervention study

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic heart failure

Interventions
Current intervention as of 25/01/2021:
The Interdisciplinary Network Heart Failure (INH) study was a two-arm parallel group randomised intervention study. Patients were randomised 1:1 into network care and usual care. Intensified patient care and management (i.e. network care) was characterised by:
1. Patient self-monitoring plus telephone-based symptom-oriented monitoring following a predefined algorithm depending on the severity of the condition.
2. Telephone-based patient-oriented education and training regarding self-care, heart failure manifestation, medications, lifestyle, psychological dimensions.
3. The intervention was performed by specialised heart failure nurses who are supervised by a physician heart failure specialist.

The INH study reported that a 6-month, structured remote patient management (RPM) intervention (HeartNetCare-HF™) did not reduce the composite primary outcome of time to all-cause death or all-cause hospitalisation in patients discharged from hospital after acute decompensation for systolic HF compared with usual care (UC); however, quality of life improved and all-cause mortality risk was significantly reduced in the RPM group.

The Extended (E)-INH study aimed to enroll a larger population to determine the effects of using the well-defined HeartNetCare-HF™ RPM strategy for 18 months on the same primary outcome, other morbidity- and mortality-related events, and patient-reported outcomes following discharge after hospitalization for acute heart failure. Efficacy was compared between an initial 6-month period of more intense RPM and the subsequent 12 months, during which less intense RPM was applied. Sustainability was assessed during prolonged prospective follow-up after RPM termination.

Previous intervention as of 15/01/2021:
This is a two-arm parallel group randomised intervention study. Patients are randomised 1:1 into network care and usual care. Intensified patient care and management (i.e. network care) is characterised by:
1. Patient self-monitoring plus telephone-based symptom-oriented monitoring following a predefined algorithm depending on the severity of the condition.
2. Telephone-based patient-oriented education and training regarding self-care, heart failure manifestation, medications, lifestyle, psychological dimensions.
3. The intervention is performed by specialised heart failure nurses who are supervised by a physician heart failure specialist.

Previous intervention as of 29/12/2020:
This is a two-arm parallel group randomised intervention study. Patients are randomised 1:1 into

network care and usual care. Intensified patient care and management (i.e. network care) is characterised by:
1. Telephone-based symptom-oriented patient monitoring following a predefined algorithm depending on the severity of the condition
2. Telephone-based patient-oriented education and training regarding heart failure manifestation, diet, psychological dimensions

Patients will be followed up for 120 months.

Previous intervention:
This is a two-arm parallel group randomised intervention study. Patients are randomised 1:1 into network care and usual care. Intensified patient care and management (i.e. network care) is characterised by:
1. Telephone-based symptom-oriented patient monitoring following a predefined algorithm depending on the severity of the condition
2. Telephone-based patient-oriented education and training regarding heart failure manifestation, diet, psychological dimensions

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measure as of 20/08/2009:
1. Death of any cause or hospitalisation of any cause (combined endpoint)

Previous primary outcome measures:
1. Death of any cause or hospitalisation of any cause (combined endpoint)
2. Quality of life

Key secondary outcome(s))
Current secondary outcome measures as of 29/12/2020:
1. Components of composite primary endpoint
2. Quality of life
3. Cardiovascular death
4. Cardiovascular hospitalisation
5. Proportion of patients treated in adherence with current heart failure treatment guidelines
6. Cost-effectiveness analyses

Previous secondary outcome measures as of 20/08/2009:
1. Components of composite primary endpoint
2. Cardiovascular death
3. Cardiovascular hospitalisation

4. Proportion of patients treated in adherence with current heart failure treatment guidelines
2. Quality of life
5. Cost-effectiveness analyses

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Previous secondary outcome measures:
1. Components of composite primary endpoint
2. Cardiovascular death
3. Cardiovascular hospitalisation
4. Proportion of patients treated in adherence with current heart failure treatment guidelines
5. Cost-effectiveness analyses

Completion date
10/10/2018

Eligibility

Key inclusion criteria
1. Age >18 years
2. Written informed consent
3. Heart failure documented by reduced left ventricular ejection fraction (<=40%) during hospitalisation and clinical signs/symptoms of heart failure (peripheral edema, pulmonary edema, rales, pulmonary congestion confirmed by X-ray, elevated jugular venous pressure, exertional dyspnea)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1032

Key exclusion criteria
1. Insufficient mental or verbal or physical ability to participate in a telephone assisted monitoring and education program
2. No telephone line installed

Date of first enrolment

01/03/2004

Date of final enrolment
10/12/2008

Locations

Countries of recruitment
Germany

Study participating centre
Nine trial sites, including two medical departments of University Hospital Würzburg plus 7 regional hospitals
Würzburg
Germany
97078

Sponsor information

Organisation
University of Würzburg

ROR
https://ror.org/00fbnyb24

Funder(s)

Funder type
Government

Funder Name
German Federal Ministry of Education and Research

Funder Name
Central Association of German Health Insurance Companies [Spitzenverband der gesetzlichen Krankenkassen Deutschlands]

Funder Name

Competence Network Heart Failure [Kompetenznetz Herzinsuffizienz]

Funder Name
German Government

Funder Name
Comprehensive Heart Failure Center Würzburg

Results and Publications

Individual participant data (IPD) sharing plan
As the researchers will perform several pre-specified secondary analyses, they do not plan to make the database available before these have been published. They will, as was the case in the past regarding the 6-month data set, make data from the database available for scientists (e.g., for reviews and meta-analyses) upon reasonable request, on which the INH coordinators will, together with the principal/corresponding author of the 120-month primary publication, decide in an individualized fashion. The primary 120-month manuscript will contain a respective statement.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	INH results	01/01/2012		Yes	No
Other publications	publication (in German) on the interventions used in this study	01/04/2009		Yes	No
Other publications	secondary analysis of participants with subclinical thyroid dysfunction	20/09/2013		Yes	No
Other publications	secondary analysis of PHQ-2 and PHQ-9 and correlation with death or rehospitalisation	01/05/2015		Yes	No
Other publications	secondary analysis of participants hospitalised for systolic heart failure	01/01/2019	27/02/2020	Yes	No
Other publications	secondary analysis of mortality reduction in depressed and non-depressed participants	01/10/2014	21/12/2020	Yes	No
Other publications	secondary analysis of prescribing	01/04/2015	21/12/2020	Yes	No
Other publications	secondary analysis of prognostic value of depressive symptoms	01/06/2015	21/12/2020	Yes	No
Other publications	secondary analysis on dysnatraemia	01/10/2012	21/12/2020	Yes	No
Other	secondary analysis of association of NPSR1 gene variants with death, rehospitalisation and healthcare utilisation	01/03	15/01	Yes	No

publications		/2017	/2021		
Other publications	secondary analysis of associations between CRP genetic variants, mortality and depression	01/07 /2018	15/01 /2021	Yes	No
Other publications	secondary analysis of prognostic potential of midregional pro-adrenomedullin (MR-proADM)	01/09 /2017	15/01 /2021	Yes	No
Other publications	secondary analysis of salivary cortisol levels	15/01 /2016	15/01 /2021	Yes	No
Other publications	secondary analysis of sex and gender differences in PHQ-9 and HRQOL responses	01/03 /2019	15/01 /2021	Yes	No
Other publications	secondary analysis of prevalence of major and minor depression	17/02 /2011	25/01 /2021	Yes	No
Other publications	secondary analysis of LVEF trajectories after acute cardiac decompensation of heart failure	02/02 /2021	27/01 /2021	Yes	No