Telemonitoring for Chronic Heart Failure: A 20-Year Journey from Concept to Standard Care in Germany

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Abstract

Chronic heart failure (CHF) is a leading cause of morbidity and mortality worldwide, with a significant burden on healthcare.

The concept of telemedicine for CHF was first proposed in the late 1990s, and since 2010, studies have demonstrated its potential to improve patient outcomes and reduce healthcare costs. Over the following decade, technologic advances and changes in healthcare policy led to the development of more sophisticated telemedicine solutions for CHF, including remote patient management (RPM) using invasive or non-invasive telemonitoring devices, mobile applications, and virtual consultations.
Many years of public funding in Germany have provided evidence that RPM improves CHF patient outcomes, such as quality of life, and reduces hospital admissions. Based on this data, the Federal Joint Committee (G-BA) decided, independently of current European Society of Cardiology (ESC) recommendations, to include telemedicine as a digital intervention for high-risk patients with reduced left ventricular ejection fraction in standard care in Germany in 2020.

The aim of this review is to illustrate the journey from the initial idea through pioneering studies that led to its implementation into standard care and to report on current experiences that have made Germany one of the leading countries in the field of cardiovascular telemedicine

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List of abbreviations

- AI: artificial intelligence
- CHF: chronic heart failure
- CHFS: Cordella™Heart Failure System
- CIED: cardiovascular implantable electronic device
- DGK: *German: Deutsche Gesellschaft für Kardiologie*, engl.: German Cardiac Society
- DGIM: *German*: Deutsche Gesellschaft für Innere Medizin, engl.: German Society of Internal Medicine
- DiGA: *German: Digitale Gesundheitsanwendungen*, engl.: digital healthcare applications
- ESC: European Society of Cardiology
- FTC: fluid tresholding crossing
- G-BA: *German*: *Gemeinsamer Bundesausschuss*, engl.: Federal Joint Committee
- HF: heart failure
- ICD: implantable cardiac defibrillator
- IQWiG: *German: Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*; engl.: Institute for Quality and Efficiency in Health Care
- LVEF: left ventricular ejection fraction
- NYHA: New York Heart association
- PAP: pulmonary artery pressure
- RPM: remote patient management

Abstract

Chronic heart failure (CHF) is a leading cause of morbidity and mortality worldwide, with a significant burden on healthcare. The concept of telemedicine for CHF was first proposed in the late 1990s, and since 2010, studies have demonstrated its potential to improve patient outcomes and reduce healthcare costs. Over the following decade, technologic advances and changes in healthcare policy led to the development of more sophisticated telemedicine solutions for CHF, including remote patient management (RPM) using invasive or non-invasive telemonitoring devices, mobile applications, and virtual consultations.

Many years of public funding in Germany have provided evidence that RPM improves CHF patient outcomes, such as quality of life, and reduces hospital admissions. Based on this data, the Federal Joint Committee (G-BA) decided, independently of current European Society of Cardiology (ESC) recommendations, to include telemedicine as a digital intervention for high-risk patients with reduced left ventricular ejection fraction in standard care in Germany in 2020.

The aim of this review is to illustrate the journey from the initial idea through pioneering studies that led to its implementation into standard care and to report on current experiences that have made Germany one of the leading countries in the field of cardiovascular telemedicine

1. Introduction: The origins of telemedicine

The history of telemedicine is closely linked to technical innovations of its time and began in the 19th century with the invention of Samuel Morse's code system. The introduction of the telephone in 1861 by Philipp Reis and its further development by Alexander Graham Bell in 1876 opened new perspectives for telemedicine by making remote diagnosis possible for the first time. In 1911, radio technology was used for the first time in maritime shipping for telemedical consultation. Since 1931, the Cuxhaven Hospital in Germany has been offering medical advice to seafarers via radio [1].

Over the last 150 years, technological innovations in telecommunications have led to new telemedical applications. However, telemedicine has been increasingly used only in the last 20 years for the outpatient care of chronically ill patients. Since the technological breakthrough in smartphones in 2007, telemedicine has become a part of our daily lives.
Telemedicine has two basic application scenarios. On the one hand, it can enable professional exchange between geographically distant service providers (so-called "doc-to-doc telecardiology"). On the other hand, a direct connection between doctors and patients can occur in the patient's home environment with the help of information and communication tools (so-called doc-to-patient telecardiology).

The actual implementation of telemonitoring in Germany, especially, was delayed due to restrictive legislation on the long-standing legal ban on remote treatment until this code of conduct was relaxed in 2018. Although direct doctor-patient contact remains the standard scenario, telemedical co-care can be added as an option. The entire replacement of outpatient medicine by telemedicine is therefore still ruled out.
All other basic characteristics, such as the personal provision of services, specialist standard, medical duty of care and confidentiality, and obligation to inform the patient about treatment risks, must be present in the case of telecardiological co-treatment and are set out in a treatment contract. The particular requirement is that patients, most of whom have no previous medical training, must be able to perform simple diagnostic procedures (e.g., blood pressure measurement and ECG recording) with sufficient precision.

Telemedicine in heart failure: a life prolonging and economic digital measure

Cardiac decompensation is the most common and prognostically significant complication of CHF, with an average survival time of approximately 2.5 years after its first occurrence [2]. Every day, approximately 1,250 patients are admitted to hospitals in Germany due to cardiac decompensation [3]. Since 2005, this has been the most common single diagnosis for hospital admissions and presents a high economic health burden [4].

The deterioration in cardiac function often begins gradually and can lead to the full clinical picture of life-threatening decompensation due to changes in certain vital parameters. Using modern sensor technology, early changes in vital signs can be detected remotely and transmitted immediately to the attending physician, leading to a sufficient doctor-to-patient telemedicine care principle. First evidence of the efficacy of home telemonitoring as a preventive strategy was provided by the TEN-HMS study (Trans-European Network-Home-Care Management System) in 2005, presenting a reduced mean duration of hospital admissions by 6 days and was significantly associated with a lower one-year mortality risk (29%) compared to usual care (45%), in patients with CHF and a left ventricular ejection fraction (LVEF) <40%. [5]

A distinction is made between invasive and noninvasive telemonitoring, depending on the type of sensor used to record typical vital signs. With invasive telemonitoring, disease-specific vital signs are recorded using active or passive-implanted devices. With non-invasive telemonitoring, vital signs are recorded daily via external home measuring devices such as scales, blood pressure monitors, external ECG measuring devices, or wearables through active self-measurement by the patient to provide the treating physicians with information about the current state of the disease.

Of the six landmark studies (→ *Figure 1*) on the efficacy of cardiovascular telemedicine, Germany provided for three of whom two were carried out with public funding, which later led to their verification as an independent treatment method: As a direct consequence, the German Federal Joint Committee has included telemedicine as a digital intervention for high-risk heart failure patients with reduced LVEF (HFrEF) in the catalogue of benefits in Germany.

This overview presents the German perspective from the initial study idea through evidence generation to implementation in standard care, reports on current experiences in Germany and provides an outlook on future developments.

2. Non-invasive Telemonitoring

Non-invasive devices (scales, blood pressure gauges, ECG device, wearables) proved beneficial in terms of multiparametric value transmission, easy handling, integrative monitoring of comorbidities (e.g. diabetes) and low costs.

Evidence for the efficacy of non-invasive cardiovascular telemonitoring was initially provided in the mid-2000s. Subsequently, a differentiation on trials according to invasive or non-invasive sensor technology has been established. Three major landmark trials, the INH- and TIM-HF and TIM-HF2 trials, were conducted in Germany and were publicly funded (by the German Ministry of Education and Research and the Federal Ministry for Economic Affairs and Climate Protection).

The INH-Study program 2004-2020

The randomized, controlled, multicenter INH (Interdisciplinary Network for Heart Failure) study program (ISRCTN23325295) investigated the effects of regular telephone-based monitoring and education conducted by HF nurses in the form of intensified care by a specialist heart failure center. The first trial phase assessed the 6-month risk of mortality and morbidity in 715 patients with a LVEF ≤ 40%, who had been hospitalized with decompensated heart failure (HF).

Even though the primary outcome of all-cause mortality at 180 days was neutral between the telemonitoring group (n=352) and the usual care control group (n=363), the separate secondary endpoints showed a significant reduction in the rate of heart-failure attributed death in the telemonitoring group. Patients in the telemonitoring group also showed an improvement in quality of life, better functional class, and better adherence to medical therapy.

A long-term evaluation as an extension of the INH trial ('E-INH study') recently showed in a larger population (n=1022) that telephone-based monitoring offered over a period of 18 months also led to a significant reduction in all-cause and cardiovascular mortality after 120 months in the group of survivors who had received RPM (33% vs. 40%, p=0.043). Also, HF-related and cardiovascular hospitalizations were significantly less frequent after 18, 36 and 60 months (-25%, -29% and -30%, respectively). As mentioned, the telemonitoring procedures did not include automated transmission of patient-recorded vital signs, but utilized post-discharge telephone-based monitoring by specialized nurses. Patient guidance relied on counseling on appropriate actions in case of suspected HF-decompensation and allowed for self-adjustments of diuretic agents in self-empowered patients.

Overall, the INH study program suggests that telephone-based monitoring and education alone can improve shot-term quality of life mortality and has a sustained long-term effect as exemplified by reduced all-cause and cardiovascular mortality, reduced hospitalizations and improved quality of life.[6] [7]

The TIM-HF Study–program 2005-2024

The TIM-HF study (Telemedical Interventional Monitoring in Heart Failure Study; NCT: 00543881) and the TIM-HF2 study (Telemedical Interventional Management in Heart Failure II, NCT: 01878630) were large randomized, controlled, open, parallel telemedical trials, investigating the efficacy of a non-invasive, multi-parameter telemonitoring in a population suffering from moderate to severe heart failure (NYHA-class II or III).

Both studies were fully publicly-funded. The key element of this telemedical care model was a telemedical center, staffed with experienced heart failure specialists and heart failure nurses, serving providing regular and emergency telemedical services 24 hours/ 7 days a week ("virtual emergency department") [8].

The TIM-HF trial was a telemedical RCT conducted between 2008 and 2010 in four German Federal States (Berlin, Brandenburg, Saxony-Anhalt, and Baden Württemberg). The main inclusion criteria were LVEF below 35 % and a history of heart failure hospitalization with 24 months prior to randomization. The primary endpoint was all-cause mortality. The study was stopped at a fixed stopping date (April 30, 2010), resulting in an individual follow-up period for every study patient. The follow-up period was at least 12 months and longest 28 months (mean 21.5 +/-7.2 months). The results regarding the primary endpoint were neutral [9]. A post-hoc analysis identified a subset of patients, that may benefit most from telemonitoring [10].

TIM-HF2 was a nationwide telemedical randomized controlled trial conducted between 2013 and 2018 in 13 German Federal States. The main inclusion criteria were based on the post-hoc analysis of the TIM-HF study. Patients were included regardless of their LVEF and had experienced a heart failure-related hospitalization 12 months prior to randomization. Altogether, 1538 patients were randomized equally to a telemedical study arm or to a control arm respectively. The study follow-up was 1 year. The primary endpoint was defined as "days lost due to unplanned cardiovascular hospitalization or due to death within one year". The secondary endpoint was defined as total mortality. There was a significant benefit of telemedical intervention regarding the primary endpoint (17.8 days lost in telemedical group vs. 24.2 days lost in the control group; 95%-CI; p=0.046). In addition, a significant reduction in one-year mortality of almost 30% could be shown in favor of the telemedical study arm (7.9% mortality rate per 100 patient years (95%-CI: range 6.14-10.10) in the interventional group vs. 11.3% mortality rate per 100 patient years (95%-CI: 9.21-13.95) in the control group. This resulted in a hazard ratio (HR) of 0.70; (95% CI: 0.50-0.96; p= 0.028) [11].

The two subsequent TIM-HF studies provided robust evidence for the efficacy of non-invasive telemonitoring in a subgroup of heart failure patients.

3. Invasive Telemonitoring using Cardiac Implantable Electronic Devices (CIEDs)

Active implants, otherwise referred to as cardiac implantable electronic devices (CIED's), offer the option for telemonitoring besides their primary function on therapy of cardiac arrhythmias via defibrillators or for cardiac resynchronization therapy. As applicated in telemonitoring, they periodically provide data on physical activity, submit ECGs and may detect changes in pulmonary impedance. However, this active home monitoring application is limited to a specific subpopulation of CHF-patients that precedingly fulfill criteria for CIED-therapy.

With the IN-TIME landmark trial leading, an era of technology-based, industry-funded study designs rather than governmental funding, paving the way for fundamental evidence and further shaping telemedical the research landscape: now device therapy-providing companies were involved as principal investigating parties.

The IN-TIME trial 2007 -2014

The IN-TIME-trial (*Influence of home monitoring on mortality and morbidity in heart failure*

patients with impaired left ventricular function; NCT: 00538356) is to date the only study that investigated on device-based multiparameter telemonitoring via active cardiac implantable electronic devices (CIED) with a positive primary endpoint for a composite score including all-cause death.
This international multicenter randomized trial was conducted at 36 centers in Israel (2 sites), Australia (1 site) and Europe (33 sites), among 26 sites in Germany and was funded by BIOTRONIK SE & Co. KG. A total of 664 patients with CHF according to NYHA class II-III, a LVEF <35% who had received implantation of a dual-chamber CIED (ICD or CRT-D) were randomized 1:1 for either standard care control arm or device-based telemonitoring additional to standard care.
The telemonitoring software installed in the CIEDs forwarded daily tracked data to the manufacturer's online platform. Data transmissions included arrhythmic events as well as parameters related to the device function. Only for the intervention group, subsequent abnormalities were further forwarded to study centers whereat heart failure nurses performed structured interviews for typical heart failure symptoms and further discussed consequent interventions with physicians.

With the primary endpoint on a "modified packer score" (incidence rate of death to any cause, heart-failure related hospitalization, change in NYHA-class, changes in quality of life) the intervention-group that received telemonitoring had a significant lower rate of occurrence of the clinical combined endpoint compared to the control arm (18.9% vs. 27.2%, respectively, p=0.013). Importantly, total mortality was also significantly lower in the telemonitoring arm (3.0% vs. 8.2% in the control arm, HR 0.36, p=0.004) whereas the rates of hospital admissions for worsening heart failure did not differ significantly between the two arms. In a post-hoc analysis, there was no interaction between the effect and the device type (ICD or CRT-D), NYHA class at enrollment or age (≤67 or >67 years) indicating a significant impact of telemonitoring across subgroups.

Thus, the IN-TIME trial demonstrated a beneficial impact of device-based telemonitoring in patients with heart failure with daily transmission. Consequently, these results are not necessarily transferable to remote monitoring platforms with less frequent transmissions. [12]

The OptiLINK-HF Trial 2009–2015

In the invasive telemonitoring OptiLink-HF study (*Optimization of Heart Failure Management using Medtronic OptiVol™ Fluid Status Monitoring and CareLink Network;* NCT: 00769457), a total of 1002 patients were included following implantation of an ICD or a CRT-ICD [13]. These CIEDs had the additional feature of measuring the intrathoracic impedance. In case of a significant decrease in thoracic impedance due to pulmonary fluid overload, the CIEDs transmitted so-called fluid threshold crossing (FTC) alerts.

Patient enrollment took place in 65 centers in Germany between October 2008 and April 2013. Mandatory inclusion criteria were chronic heart failure with NYHA class II or III stages, a LVEF <35% and either heart failure hospitalization in the past 12 months, intravenous diuretic medication for outpatient treatment, or an increase in natriuretic peptides within the past 30 days.

The patients were randomized in a 1:1 fashion having the telemedicine function turned on or off. Physicians had to respond with a pre-specified intervention algorithm by phone within 2 working days [14]. During phone contacts, changes regarding body weight, medication, and symptoms of decongestion were addressed. The initiation of therapeutic measures was left at the physicians' discretion. This also included no actions at all or reprogramming the FTC alert

threshold. If FTC alerts persisted over 12 days, patients were asked for an in-office or in-hospital visit.
The follow-up for all study patients was 18 months with the possibility of a re-informed consent to prolong the follow-up period until the last patient had completed the study visit after 18 months. This resulted in a mean follow-up period of 22.9 months.

The primary endpoint was the rate of death from any cause and the rate of cardiovascular hospitalizations. Notably, neither the primary composite endpoint nor its components were met. Major study limitations included technical issues, 24% of the impedance alarms could not be transmitted to the treating physicians, and inappropriate answers to the alerts in 40 %. The latter included no patient contact at all (12.4%), patient contact exceeding 2 working days (10.8%) (especially during weekends and public holidays (4)) or no appropriate medical intervention (32.8%).

Interestingly, a post-hoc analysis of the OptiLink-HF trial suggested significant prognostic effects by impedance-based telemonitoring, when alert transmissions were handled appropriately [15]. Moreover, the intervention significantly decreased the primary endpoint in patients with preserved renal function, but not in those with chronic kidney disease (CKD) [16], underlining that timely and resolute management of alert transmission is particularly important in these vulnerable patients [17].

4. Invasive-hemodynamic telemonitoring

The alterations of intracardiac filling pressures as the ideal surrogate of incipient congestion is not well reflected by body weight. The invasive hemodynamic telemonitoring offers the advantage of earlier detection of impending events of a cardiac decompensation [18]. Regardless of the underlying technical devices, however, a reliable and prompt integration into telemedical center workflows is considered crucial for therapeutic effectiveness
Intracardiac filling pressures may be monitored via tracking the pressure of the pulmonary artery (PAP)/ -right ventricle or left atrium. These implants allow to transmit tracked values in a “passive” manner upon query with a wireless external readout device.

The CardioMEMS™ HF System

The electrode- and battery-free PAP sensor *CardioMEMS*™ (Abbott Laboratories, Abbott Park, IL, USA) is implanted in a proximal branch of the pulmonary artery and calibrated to the individual patient. Changes in pulsatile flow can be transformed into a pressure derivate and wirelessly transmitted to a remote dashboard, e.g., at a telemedical center. Daily measurements have to be started actively by the patient, and a specialized staff regularly interrogates the PAP trends accruing over time, in order to device whether and which action has to be taken. In the Abbot-funded CHAMPION trial (NCT00531661), conducted in the U.S. and Canada [19], 550 patients in NYHA functional class III and irrespective of LVEF had PAP sensors implanted. CHAMPION reported a 39% risk-reduction of heart failure-related hospitalization after six months in patients who received physician-led interventions upon assessment of obtained PAP-values, compared to the control group [19]. These effects were sustained after 12 months and were consistent in the non-randomized 3-year extended follow-up period [20]. The prospective MEMS-HF registry (*CardioMEMS*™ European Monitoring Study for Heart Failure) had an observational design and yielded comparable effects when used within the European healthcare system [21].
These findings were corroborated by the pre-COVID-19 impact analysis of the GUIDE-HF trial (NCT03387813) studying 1000 patients in NYHA class II or III from the U.S. [22] and the recent MONITOR-HF trial (NTR7673) conducted in 348 NYHA class III patients in the

Netherlands [23]. Both trials indicated a sizeable benefit of PAP-guided management on heart failure hospitalization rate compared with the control group.

The CardioMEMS™ HF System in Germany: The PASSPORT-HF-trial

As aforementioned, the Federal Joint Committee/G-BA evaluates medical innovations for inclusion in the medical services covered by health insurances. Since major differences in health care systems between the U.S. and Germany are apparent, the G-BA decided, as a novelty, to directly fund a telemedicine randomized-controlled trial in 50 study centers. The still ongoing PASSPORT-HF-trial (*Pulmonary Artery Sensor System Pressure Monitoring to improve Heart Failure Outcomes*; NCT: 04398654) aims to recruit 554 patients in NYHA class III and with a heart failure hospitalization within the last 12 months.
PASSPORT-HF is investigating whether PAP-guided and HF nurse supported care utilizing daily monitoring of PAP values with the *CardioMEMS*™-system (Abbot) reduced the number of unplanned HF-related hospitalizations or all-cause death after12 months.

CHF patients are being randomized in a 1:1 ratio to either device-implantation or (in contrast to the CHAMPION trial) no device implantation in the control arm. Both groups are receiving structured telephone support from HF-nurses next to guideline-compliant drug therapy, which exceeds standard practice in Germany. Therefore, PASSPORT-HF will evaluate whether the so far reported benefits of PAP-guided hemodynamic monitoring as a novel HF management tool in routine outpatient telemedical care can be replicated in the German healthcare setting. First study results are expected in 2026 [24].

Recent innovations: The *Cordella™* HF management system

The *Cordella™HF management System* (CHFS, Cordella, Endotronix Inc., Chicago, IL, US) consists of an implantable and battery-free PAP sensor and an external handheld patient reader. The system was investigated in the SIRONA study program (NCT: 03375710).
As such, it is first to enable parallel recording of both invasive PAP data and external measured parameters (blood pressure, heart rate, body weight, oxygen saturation). Therefore, the system provides a more comprehensive picture of a patient's state of compensation to the HF care team and allows the patient to view his/her trending data using an easy-to-use handheld readout device for PAP measurement. Unlike the *CardioMEMS*™ HF system, PAP measurements can be carried out in different body positions and under stress conditions. This is important as patients reported a clear preference for measurements in a seated position [25].

The *Cordella*™-system has initially been evaluated as a first-in-human study of 15 patients, the PAP difference 90 days after implantation yielded no difference between values derived by the *Cordella*™ sensor and right heart catheter. Of note, patient compliance with daily remote monitoring was >98% [26]. The SIRONA-2 multi-center, single-arm, open-label approval study (NCT: 03375710) involved 70 HF patients in NYHA class III at 4 sites in Ireland and Belgium and also 3 German centers.

The primary efficacy endpoint that compared the *Cordella™* PAP sensor measurement to established catheter-derived reference pressure at 90 days was met (mean PAP difference 0.0 to 2.9 mmHg, p=0.003), remaining in good agreement up to 12 months of observation. There were no reports of sensor failures or death within the 90-day period [25] and improvements in NYHA class and 6-minute walk distance were observed [27]. Hence, the *Cordella*™ management system appears feasible and safe and is currently under investigation in the PROACTIVE-HF single-arm study (NCT04089059), which has prespecified safety and effectiveness endpoints to provide objective evidence of a similar risk-/ benefit profile to the *CardioMEMS*™system in 450 patients in NYHA class III.

5. The regulatory process: From trials to standard healthcare in Germany

Telemonitoring in patients with CHF as a digitally supported type care, has been recognized as an independent examination- and treatment method by decision of the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) in March 2021. [28] Consequently, telemonitoring became a standard health care service for this patient group in Germany [29]

Since 2009, health insurance is compulsory for all German residents as ruled by the German Insurance Contract Act [30]. As of 2022, approximately 87% of residents are covered by statutory health insurance and approximately 10% by private insurance [31]. Both types offer telemonitoring as a service, however private insurers define new aspects regarding current indication criteria (*see Table 1*).
Reimbursement by (statutory) health insurance companies requires a prior assessment of benefit, necessity and cost-effectiveness. For the evaluation of digital care services such as telemonitoring, the G-BA also has the statutory task of conducting a qualitative benefit assessment. The submission of research projects for assessment by the G-BA is subject to a particularly strict "one-shot" strategy, as projects can only be submissed once.

Research on the efficacy of telehealth interventions in the care of patients with CHF is inconsistent: Reasons for the different clinical endpoints include differences in the telemedical systems used (invasive measurement sensors vs. non-invasive monitoring) or different concepts of guided care (such as the involvement of "heart failure nurses"). In addition, different response times to abnormal transmitted values were defined (during regular consultation hours vs. 24/7 care by a telemedicine center).
Despite these differences in the study design, the German TIM-HF2 landmark trial, among others, identified high-risk patients with a 12-month history of HF-related hospitalization as the population that benefits most from telemedical co-care.
The fact that there is no treatment benefit in the absence of such a recent HF hospitalization is an important evidence-based selection criterion for the indication for telemonitoring, thereby, avoiding unnecessary resources [29].

Since 2016, the Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG), as the highest joint self-governing body of the German healthcare system operating, has been investigating the benefits of invasive telemonitoring with active implants and non-invasive telemonitoring in CHF on behalf of the Federal Joint Committee. The aforementioned IN-TIME trial for invasive telemonitoring and the German TIM-HF and TIM-HF2 trials for non-invasive telemonitoring formed the basis of an assessment regarding additional healthcare benefits.[11, 12, 32] In its assessment of October 2019, the IQWiG identified a statistically significant reduction in cardiovascular mortality through telemonitoring as a sufficient additional benefit. [33]
According to the above-mentioned G-BA decision, telemonitoring is currently only indicated for CHF patients with reduced LVEF. This selection criterion is inconsistent with current trial data, that also revealed a benefit for CHF patients with a preserved LVEF [11]. A re-evaluation by the G-BA and, ultimately, by the IQWiG for translation into medical care is currently pending.

6. The role of medical scientific societies in telemonitoring implementation processes

The German Cardiac Society (Deutsche Gesellschaft für Kardiologie, DGK) provides an

important basis for the development of collaborative projects in telemedicine for patients with CHF. In 2005, the DGK founded a telemedicine working group (Working Group 33) that also deals with the certification criteria for telemedicine centers [34]. Accordingly, a position paper on the certification processes ensuring quality standards for telemedical centers that are aligned with legal requirements has been published in 2022. [35]
A thorough understanding of the available technical capabilities is essential for the effective collaboration of different study groups and the development of joint projects: Therefore, the working group on CHF (Working Group 10) developed guidelines for patients planning long-distance travelling [36]. As a straightforward and intersecting approach to telemedical surveillance, remote monitoring of implanted devices (such as pacemakers, ICD's, and implantable cardiac monitors) has been recommended and further implemented by the ESC. [37-39]

Another important step toward representing professional interests at the national level was the establishment of the "*Digital Transformation in Internal Medicine*"-commission of the German Society of Internal Medicine (Deutsche Gesellschaft für Innere Medizin, DGIM) in 2019. The DGIM represents the largest medical society in Germany, founded in 1882 and steeping in tradition with over 30,000 members [40-42]. First in 2014, the DGIM published guiding principles for the implementation of telemedical service provision. [43] The commission further serves its self-conception as a platform to impart literacy, offer training opportunities as well as scientific support services.

On an European perspective, the ESC defined telemedical care concepts in a position statement in 2015 as one of seven application areas of e-Health in cardiology [44]. For reasons of technical developments and updated evidence the paper was yet of preliminary appeal, for that matter the *ESC Digital Health Committee* had been founded in 2016 and is continuously discussing scientific updates for that matter. The recent guidelines of the ESC on the diagnosis of acute and chronic heart failure (2021) distinguish between hemodynamic, *invasive* telemonitoring using implants measuring PAP and *non-invasive* telemonitoring with external measuring devices, resulting in the issue of class II-B recommendations for both telemedical technologies.[45]

7. International co-operations

The German research and development (R&D) project of telemedicine for HF patients was always connected to international developments in this field. A good example is the German-Austrian Project "Telemed5000" (Project Number: FKZ-01MD19014A), which investigated the applicability of artificial intelligence (AI) in the workflow of a telemedical center with a budget of approximately 2,4 million Euros between 2019 and 2023. This project was founded by the German Federal Ministry of Economic Affairs and Climate Action and co-founded by the Austrian Federal Ministry of Climate Action, Environment, Energy, Mobility, Innovation and Technology. [46]

There was and there is an intensive international exchange about scientific results regarding telemedicine in HF patients and about German experiences in the implementation process, in particular with EU-neighboring countries. For example, the *German Foundation for the Chronically Ill* (Deutsche Stiftung für chronisch Kranke) organized a round table of experts from seven European countries (France, Germany, Italy, Poland, Spain, Netherlands, and United Kingdom) in December 2023 in order to review the current state of telemedicine within the participating countries, further learning from each other and providing an impetus for European co-operation (https://www.dsck.de/aktuelles)
An establishment of reliable regulations, an overcoming of regional differences, the

redefinition of roles and processes, the personalization of healthcare services, the promotion of innovation and research, the use of AI and, finally, an efficient management and safeguarding of healthcare data were identified as key levers for further developments of telemedicine.

8. Current practice in Germany

An estimated 150,000 to 200,000 patients with CHF in Germany are currently eligible to telemedical co-care [47]. In addition, the G-BA in Germany has defined criteria for the inclusion of current cardiovascular telemonitoring (*Table 1*).

Accordingly, care is provided by the primary physician (primary physician or specialist in internal medicine or cardiology) in cooperation with a consulting physician (cardiologist) in the telemedicine center. Therefore, the entire care process is considered for outpatient settings only and completely separated from in-hospital stakeholders.
Cardiologists who attempt to provide telemonitoring need to hold a license for treating patients in the setting of public health insurance. The presence of a technical infrastructure and a license for the follow-up of cardiac implantable electronic devices (CIEDs) are mandatory for setting-up a telemonitoring center.[28, 48]

After a patient has consented to telemonitoring, a training into the proper use of the issued equipment is being performed by qualified HF nurses. Thus, an adequate patient adherence builds the profound basis for adequate measurements and subsequent data transfer. However, monitoring of CIEDs is automated with individually programmed alerts being transmitted as soon as there is connection between the CIED and the transmitter. An 80% data transmission rate is mandatory and has to be reported by the telemedicine center on an annual basis. The telemedicine center is required to evaluate patient data on a minimum of 5 days per week or on a daily basis for severely ill patients (“intensified monitoring”). If a response is required (such as a change in medication), the telemedicine center is obliged to contact the primary care physician or interact directly with the patient if the primary care physician is not available. These reactions have to occur within prespecified time frames: The processing of an alert must not exceed 24 hours; the transmission of a subsequent clinical need of action may take a maximum of 48 hours for reaching the primary attending physician (*see figure 3*).
Furthermore, a quality assurance program for telemonitoring is implemented focusing on adherence to guidelines, daily review of data, alarm management or hospitalizations for decompensated heart failure and other scenarios.

9. Further digital applications in Germany (DiGAs)

Digital health applications present prescription-enabled mobile applications (apps) which are distinctive to classic telecardiology that provide daily evaluation of transferred values and derive subsequent consequences: These apps represent the third pillar of patient management, attributing mobile health and have the primary intent to enable patients for self-management of chronic diseases, especially concerning lifestyle and behavioral modifications.
The central website of the German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM) provides a directory of available digital health apps (*https://diga.bfarm.de/de*) in 12 different medical field-attributed associated categories that carry relevant information for patients and providers. To date, only one DiGA “*ProHerz*” has provisionally been approved for HF patients. However, it is known that long-time engagement in digital apps is only met by a small number of users, as for instance 30-day retention rates in patients using mental health apps only scored 3.3%[49] .
To enhance adherence, future “DiGAs 2.0” including artificial intelligence (AI)- applications

promise for a feasible transmission of vital parameters tracked by wearable devices that might allow for more effective therapies in remote HF compensation analysis, but require thorough scientific evaluation. The initial narrative of a DiGA to be used by the patient alone, is ongoingly discussed for matters of higher scalability concerning remote monitoring and a more detailed integration in the medical practises of general practitioners and specialists.

10. Upcoming challenges

Unmet questions of remote patient monitoring

Telemonitoring is an effective technology in terms of availability, accessibility and affordability, while improvements in CHF outcomes through telemedicine have not been demonstrated for all different technologies and devices available. Refining the current evidence remains challenging due to unresolved questions about the most appropriate monitoring technology for the individual patient, the best time to start and, most importantly, the duration of telemonitoring after cardiac decompensation. [50]
Furthermore, there is a need to incorporate current evidence for special patient populations such as heart failure patients with a preserved ejection fraction [51], into the catalogue of services provided by statutory health insurance without restarting the entire authorization process.
In contrast to the introduction of a new drug therapy, the transfer of a digital therapy from a controlled study set-up to routine healthcare is much more complex. For the introduction of non-invasive telemedicine in HF, the publicly funded prospective phase IV registry study ("TIM-HF4", Telemedical Interventional Management in Heart Failure 4) will begin in 2025, which will investigate patient acceptance and the effectiveness of non-invasive telemonitoring in heart failure under real-life conditions with regard to repeated hospitalizations due to heart failure and death from any cause as well as health economic criteria.
A transferability of telemonitoring to other cardiological indications has not been sufficiently addressed in scientific trials yet. Telemonitoring could be feasible for clinical settings in terms of improved discharge processes (e.g. accelerated patient discharge after rhythmological intervention) and aftercare. Notably, in terms of a faster and reliable up-titration of guideline directed medical therapy, taking into account of patients' clinical tolerability and vital signs, telemedical supervision might be highly beneficial, as the STRONG-HF trial uncovered a markedly reduced risk for HF readmission and reduced symptoms when guideline directed medical therapy was up-titrated within 2 weeks of discharge accompanied by monitoring of the clinical status and evaluation of laboratory values. [52]
However, concerning a prehospital setting, the currently ongoing randomized, controlled ResKriVer-TAVI study, funded by the Federal Ministry for Economic Affairs and Climate Action (German Clinical Trials Register DRKS:00027842), is investigating, whether telemedical interventional management improves clinical outcomes (cardiovascular hospitalization, death of any cause) in patients with aortic stenosis awaiting TAVI (transcatheter aortic valve implantation) [53] .

While feasibility studies address the proof of concept of latest technologies, there is an unmet need for randomized trials to test the clinical efficacy of cutting-edge telemonitoring devices and their eventual integration into routine practice. Hence, it remains unclear whether non-invasive measurements via wearable devices are an equally efficient tool in comparison to implanted cardiac devices. Also, combining methods with integration of multiple sensors has yet to be tested for superiority against a single sensor approach.

AI-supported applications in telemonitoring and remote patient management

With an increasing number of patients entitled to telemedical care, machine learning tools offer particular potential for the challenges of numerical upscaling or the pre-processing of complex health data from various sources. To date, triaging of vital parameters is an already established tool. In the future, pattern recognition will further refine prioritization and prediction of interindividual decompensation thresholds.
Nevertheless, AI-applications are currently not eligible for standard cardiovascular telemedicine care. With the entry into force of the European AI-Act in March 2024 [54], clear transparency requirements and certain obligations for higher risk AI-applications will open a broad spectrum for research into applications in telemonitoring patient care.
AI is also a promising tool for identifying novel HF parameters: AI applications could merge smartwatch-based data with already established intra- and extracardiac device monitoring data. A real-time-analysis of wearable-derived intrinsic hemodynamic changes (via analysis of heart rhythm, heart rate, level of activity, pedometer, oxygen saturation) could further improve patient-related outcomes by instant-alerting of the telemedical center.

The telemedical sensor system will likely be complemented by automated speech analysis to detect pulmonary congestion, as promising data showed a prediction of HF-events up to 3 weeks in advance.[55] The "*Cordio HearO*" smartphone application was introduced in a first pilot study including 40 patients with acute cardiac decompensation[56]. This innovative strategy is ongoingly investigated as part of the "Telemed5000-Stimme" observational study (DRKS00020763) in patients on regular hemodialysis [57] in Germany as well as the "VAMP-HF"-study (*AI-based Voice Analysis for Monitoring Patients Hospitalized with Acute Decompensated Heart Failure)* in patients with acute decompensated heart failure at the Deutsches Herzzentrum der Charité and the US Mayo Clinic [58] .
Besides their promising transformative potential, the implementation of AI-tools in cardiovascular telemonitoring remains a challenge in terms of ethical scenarios and data protection.

11. Conclusion

The development of telemedicine for the care of HF patients in Germany has been an extremely long and difficult process, paved by public funding. Important milestones were major pioneering studies such as the TIM-HF2 and IN-TIME trials, which demonstrated the effectiveness of telemedicine approaches using different technological methodologies. The success was largely due to the close co-operation between research and technology developers, who created innovative solutions for clinical practice. One major hurdle that had to be overcome was the traditionally strong separation between inpatient and outpatient care settings in Germany.
With the gradual introduction of telemedical services for HF patients, research in this area has not come to an end. Rather, the knowledge gained will be used to continuously improve care and drive forward the digital transformation in the healthcare system. Care research approaches such as the forthcoming TIM-HF4 study play an important role in the evaluation of the efficacy for non-invasive telemonitoring in a real-life setting in terms of health economic criteria.
As a future approach, the establishment of telemedical care for HF patients across Europe is likely to benefit from experiences gained in Germany. Despite going a long way, these efforts have led to a significant improvement in the care of patient with HF.

Conflicts of interest

None to declare.

Author contributions

SSp and FK equally drafted the manuscript. Contributing authors GH, KK, MB, BA, MMö, MMi, SSt, ML, DR, RB, AA, SvH, TH, CA, SSa, TB, JG, MK, GE, CV, SW, CM, JW, BZS, ND, JZ, FK. FK und SSp supervised manuscript writing and provided continuous guidance. All authors read and approved the final manuscript.

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Figure legends

Figure 1: Highlighted trials and RCT's on telemonitoring from 2019-present (upper panel). Color-coded main outcome of further RCT's as further analyzed in the MONITOR-HF-study [23]. Trials identified by their respective names or acronyms. Trial-results were or will further be influenced by development of telecommunication technologies (lower panel)

Figure 2: Selected types of sensors used in telemonitoring (CIED: Cardiac Implantable Electronic Devices)

Figure 3: Components of telemonitoring in heart failure according to the G-BA approval in Germany.

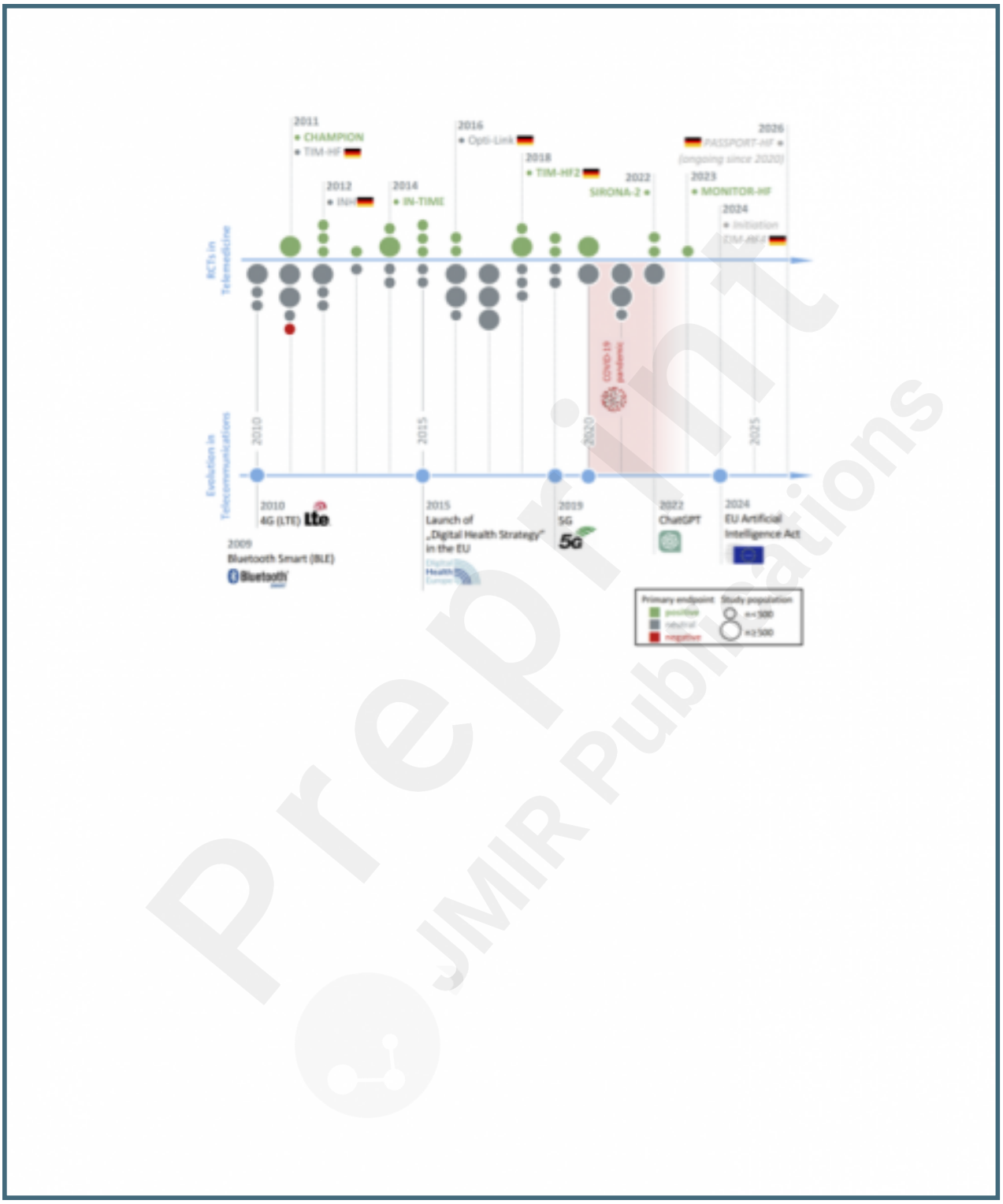
– NYHA II-III stage heart failure with a present LVEF <40%
– implanted cardiac device (ICD, CRT-P/-D) or HF-hospitalization due to cardiac decompensation in the past year
– Present treatment according to current guidelines (guideline directed medical therapy, GDMT)
– Absence of identifiable factors that compromise the transfer of monitoring data or that would interfere with patient self-management
– *if other prerequisites are fulfilled: patients with a private health insurance who suffer CHF and exhibit a LVEF > 40%; also including hospitalization for decompensated HF within the last 12 months

Table 1: Current inclusion criteria for heart failure telemonitoring (according to G-BA decision and *reimbursement for private insurance):

Supplementary Files

Figures

Highlighted trials and RCT’s on telemonitoring from 2019-present.



Selected types of sensors used in telemonitoring (CIED: Cardiac Implantable Electronic Devices).

Components of telemonitoring in heart failure according to the G-BA approval in Germany.