









Are Hospital Admissions (Costs) and Mortality Rate Impacted by Guideline-driven Treatment of Heart Failure?: A Comparison between Participants in the "CorBene" CMP and Standard-care Patients on the **Basis of Propensity Score Matching**

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Abstract

Keywords

- ► angioplasty
- ► artery
- ► atherosclerosis
- ► cardiac catheterization
- ► cardiovascular disease
- cardiovascular risk factors
- ► coronary intervention

Heart failure (HF) is one of the most common diagnoses on admission to hospital in Germany, and one which incurs high costs. Integrated care in case management programs (CMPs) aims to improve treatment quality in the sense of guideline-driven treatment, while reducing hospital admissions, hospital costs, and mortality. A total of 1,844 patient data records from 11 German statutory health insurance companies enrolled in the CMP (intervention group [IG]) were compared with 1,844 standard-care patients (control group) using propensity score matching. The two groups were assessed over three follow-up observation periods regarding the endpoints' treatment costs, hospitalization rate, indicators for treatment quality (diagnostics, physician contact), and mortality. The evaluation revealed no significant differences regarding overall costs. The IG incurred significantly higher outpatient costs, but the medication costs and inpatient costs were not significantly different. There were also no significant differences in the number of hospital admissions. Patients within the CMP had significantly more frequent contact with a cardiologist, and underwent echocardiographic examination significantly more frequently. Mortality during the first follow-up observation year was considerably more favorable for the IG. There are indications that treatment quality is improved in HF patients.

Heart failure (HF) poses a major global clinical and public health problem involving considerable expenditure, as well as increased morbidity and mortality. According to the latest evaluations, the prevalence of HF in Germany is between 4 and 6%.^{2,3} Due to the progressive aging of society

and generally improved medical care, these figures are expected to rise further in the coming years.⁴

HF is increasingly the most common inpatient hospital diagnosis, with approximately 40,000 admissions in 2016.⁵ In patients hospitalized due to HF, the readmission rate

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Table 1 Diagnostic-therapeutic modules in the CorBene program

GP	Module 1	 Medical checking of eligibility criteria/clinical examination; in cases of suspected HF, referral to cardiologist (no documentation required) Introduction of CorBene, handing out of information material Agreement regarding further treatment/feedback from enrolling network partners/GP
Cardiologist	Module 2.1	 Cardiological-diagnostic complex; enrolment of patients and documentation of screening examination If appropriate, instigation of BNP measurement
	Module 2.2	Instigation of BNP and/or medication titration
	Module 2.3	Gap between reassessments according to NYHA classification, as well as corresponding checkup and subsequent documentation

Abbreviations: BNP, B-type natriuretic peptide; GP, general practitioner; HF, heart failure; NYHA, New York Heart Association.

within 3 months of discharge was just under 17%, mortality after 1 month almost 6%, and after three more months twice as high.⁶ These data are consistent with evaluations by European registers.⁷⁻⁹ In 2019, according to ICD-10 I50, heart failure was responsible for 3.8% of all deaths from ICD-10-listed diseases.¹⁰ The costs directly caused by HF have continually increased in the past years, for Germany reaching €5.28 million in 2015.¹¹

Despite its great relevance, the past treatment quality of HF has been poor. ACE inhibitors and $\beta\text{-blockers}$ are among the medication groups most frequently prescribed, 10 and yet these figures bear no relation to the recommended dosage. For example, according to studies from 2013, only 28% of patients took an ACE inhibitor following the required dosage, and the figure for $\beta\text{-blockers}$ was only 17%. 12 Moreover, only approximately 10% of these patients saw an ambulatory cardiological specialist. 13 Patients who received only half the recommended dosage of ACE inhibitors and $\beta\text{-blockers}$ display a higher risk of mortality and hospitalization. 14

The studies show that multiprofessional treatment reduces mortality and hospital admissions, while also improving adherence to medication recommendations. ¹⁵ In cases with the highest degree of evidence, the European Society of Cardiology recommends enrolment in a case

management program (CMP).¹⁶ One of these CMP is the BNK (Professional Association of Cardiologists in Private Practice) program CorBene. Following appropriate information and consent, patients with systolic and diastolic HF are enrolled by their physicians. One prerequisite is close interaction between clinical physician, cardiological specialist, general practitioner (GP), and rehabilitation specialist. Corresponding modules have been developed (**~Table 1**).

Participating GPs can refer their patients to a cardiologist within 7 days. The specialist then divides patients up into New York Heart Association (NYHA) degrees of severity, which in turn determines the reassessment interval. NYHA classification is an established procedure for dividing HF into a total of four stages, where assignation is oriented to symptoms and functional capacity (**~Table 2**).

Telemedicine and telemedical monitoring can be prescribed. The GP receives precise notifications and a recommendation for guideline-driven treatment. There is a positive list which takes into consideration all guideline-driven treatment options and which is continually updated to state-of-the-art standards. ^{16,17} A study on the care of HF patients within a CMP has already shown a reduction in hospital admissions. The average annual hospitalization costs could likewise be reduced compared with standard-care patients in the control group (CG). ¹⁸

Table 2 New York Heart Association classification with reassessment intervals

NYHA stage	Symptoms and functional capacity	Reassessment intervals
I	 Heart disease with no limitation of physical activity Ordinary physical activity does not cause undue fatigue, palpitations, dyspnea, or angina pectoris 	Once a year
II	 Heart disease with slight limitation of physical activity Comfortable at rest or low-level physical activity Ordinary physical activity causes undue fatigue, palpitations, dyspnea, or angina pectoris 	Twice a year
III	 Heart disease with marked limitation of physical activity during routine tasks Comfortable at rest, but less than ordinary physical activity causes undue fatigue, palpitations, dyspnea, or angina pectoris 	Four times a year
IV	 Heart disease with inability to carry out any physical activity without discomfort Symptoms at rest, bedridden 	Every 9 weeks (maximum 6 ×/year)

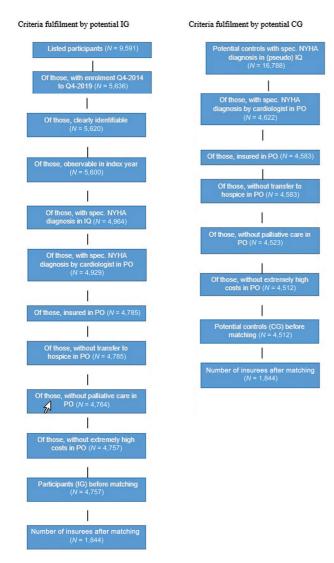


Fig. 1 Flow chart showing population selections. CG, control group; IG, intervention group; NYHA, New York Heart Association; PO, prior observation period.

Hypothesis

"CorBene" participants differ from HF patients receiving standard care and not participating in the program with regard to (1) costs, (2) hospital admissions, (3) indicators for treatment quality, and (4) mortality.

Methods

Study Design

The base data for this comparative cohort study are billing data of insurees from 11 health insurance companies participating in CorBene, and the evaluation data. From enrolment in the CMP or from a randomly assigned index date, persons with HF are observed for a maximum follow-up observation period (FUO) of 3 years. A period of 1 year before the (random) index date is used for the collection of sociodemographic and clinical variables.

There follows a descriptive and hypothetical evaluation (inferential statistics) regarding differences existing

between participants in the CorBene program or intervention group (IG) and nonparticipants in the CG. For the IG, a CG of identical structure is created from the nonparticipants using propensity score matching (PSM). Both cohorts are followed prospectively from the time of intervention. Overall, IG and CG are compared over three different observation periods (FUO 1, FUO2, FUO3). The two groups are compared with regard to the following endpoints:

Costs

- · Costs for treatment by ambulatory physicians
- Outpatient costs (cardiologists)
- Inpatient costs (with overnight stays)
- · Costs for medication indicated for HF
- Overall costs (outpatient, inpatient, medication)

Hospitalization Data

Number of (overnight) inpatient cases within each observation period

Treatment Quality

- Outpatient utilization: comprising all outpatient physician-patient contacts on the basis of contact-dependent Einheitlicher Bewertungsmaßstab (EBM) codes (German catalogue of uniform evaluation standards for reimbursement of outpatient services)
- Qualitative care aspects: echocardiographic examinations; patients with at least one outpatient or inpatient codification

Mortality

· Patients who died during the observation period

Study Population

The IG is the group of insurees who began participation in CorBene between October 1, 2014 and December 31, 2019. The quarter year when enrolment first took place is defined as the index quarter. The potential control group (CG), from which a comparative group is formed using PSM, consists of insurees not taking part in CorBene during the observation period (January 1, 2014–December 31, 2020). These insurees are assigned a random pseudo-index quarter based on the index quarter distribution of the IG.

Selection of insurees for the study is dependent on the following inclusion and exclusion criteria.

Inclusion Criteria

- Existing insurance policy with one of the health insurance companies participating in CorBene and the evaluation during the three quarters prior to the index quarter and the index quarter itself
- HF with specified NYHA stage (I–IV) during the index quarter through codification of confirmed ambulatory diagnosis by an ambulatory cardiologist or ambulatory GP
- HF with specified NYHA stage diagnosed by a cardiologist during the index quarter or in the three quarters prior to the index quarter

- One of the following diagnostic measures performed in the index quarter, in the quarter prior to the index quarter, or in the quarter following the index quarter:
 - echocardiography
 - o cardiac catheterization
 - o magnetic resonance imaging

Exclusion Criteria

- Incomplete observability (e.g., through death, change of health insurance company, etc.) in the three quarters before the index quarter, the index quarter, and the first day after the index quarter
- Transfer to a hospice in the three quarters before the index quarter or in the index quarter
- Palliative care in the three quarters before the index quarter or in the index quarter
- Extremely high costs in the three quarters before the index quarter or in the index quarter (combined sum from outpatient sector, outpatient dialysis, outpatient hospital treatment, inpatient sector and medication >€100,000).

Matching Procedure and Statistical Analyses

Group differences were quantified regarding numeric variables using the two-sided *t*-test, and regarding binary or categorical variables using the chi-square test. The effect size was ascertained using standardized mean difference (SMD) in the form of Cohen's d.

To avoid distorted estimation of causal associations of the analyzed data, the confounders were controlled using PSM. PSM is used for selection of a structurally identical CG. ¹⁹ Each insuree in the IG was assigned an insuree in the CG to match the

observed confounders and to make participation in CorBene the sole distinction. Confounders are the parameters associated with the influencing and target parameters to be investigated. In this study, the propensity score expresses the conditional probability for participation in CorBene. Assignation is performed using one-to-one matching without exceeding a caliper of 0.2 of the standard deviation. Participants who could not be matched to a nonparticipant with a similar propensity score are of no further interest.

Differences between IG and CG before and after matching are tested by observing the balance between the matched groups using SMD, which should be below 20% for all control variables.

With the difference-in-differences method (DID), the change over time which is individual to one patient is taken into account when comparing IG and CG. Existing differences are partialled out prior to the intervention. In this way, only the intervention effect is viewed. The difference in increase between IG and CG can be interpreted as an effect of the intervention.

The evaluation was performed using the program R in version 4.0.2.

Results

After matching, 1,844 insurees from each of the IG and CG were compared. In total, 3,688 patients were therefore included, taking into account the criteria described previously. The study population of the IG had a mean age of 70.5 years and was predominantly male (66.27%). **Table 3** shows the basic data of the entire random sample for the study following PSM.

Table 3 Basic data of random sample

Parameter	IG (n = 1,844)	CG (n = 1,844)	<i>p</i> -Value	SMD		
Age at time of reference, AM (SD)	70.5 (±10.7)	70.3 (±12.3)	0.578	0.0183		
Percentage female, % (N)	33.7 (622)	34.2 (630)	0.781	-0.009		
Heart failure stage % (N)						
NYHA I	22.99 (424)	22.99 (424)	1	0		
NYHA II	44.6 (823)	44.6 (823)	1	0		
NYHA III	24.8 (458)	24.8 (458)	1	0		
NYHA IV	7.5 (139)	7.5 (139)	1	0		
Obesity, % (N)	34.22 (631)	32.48 (599)	0.264	0.0368		
Hypertension, % (N)	92.41 (1,704)	92.52 (1,706)	0.901	-0.004		
Diabetes, % (N)	33.81 (1,608)	41.30 (1,859)	0.919	-0.155		
Implantable cardioverter defibrillator (ICD), % (N)	1.95 (36)	2.22 (41)	0.565	-0.019		
Charlson comorbidity index, AM (SD)	3.83 (±1.7)	3.82 (±1.8)	0.781	0.009		
Number of different active agents/ medication indicated for heart failure, AM (SD)	2.71 (1.4)	2.75 (1.41)	0.385	-0.029		
Number of (overnight inpatient) hospital admission cases for heart failure, AM (SD)	0.1 (0.34)	0.09 (0.34)	0.663	0.014		

Abbreviations: AM, arithmetic mean; CG, control group; IG, Intervention group; N, number; NYHA, New York Heart Association; SD, standard deviation.

Table 4 Outpatient, inpatient, and medication-related costs

Parameter	IG	CG	<i>p</i> -Value	SMD	DID	
Outpatient costs (total), €						
PO (N = 1,844)	1,290	1,260	0.23	0.04	-	
FUO1 (N = 1,844)	1,501	1248	<0.01	0.23	223.59	
FUO2 (N = 1,515)	1,344	1,125	<0.01	0.12	180.36	
FUO3 (N = 1,004)	1,347	1,132	<0.01	0.12	162.16	
Inpatient costs (Total), €	·					
PO (N = 1,844)	3,540	3,379	0.46	0.02	-	
FUO1 (N = 1,844)	3,466	3,747	0.38	-0.03	-442.82	
FUO2 (N = 1,515)	3,092	3,535	0.31	-0.04	-584.80	
FUO3 (N = 1,004)	3,338	3,614	0.56	-0.03	-419.47	
Medication-related costs, €						
PO (N = 1,844)	1,003	1,010	0.86	-0.01	-	
FUO1 (N = 1,844)	1,286	1,282	0.96	0.00	10.94	
FUO2 (N = 1,515)	1,327	1,184	0.25	0.04	149.66	
FUO3 (N = 1,004)	1,354	1,260	0.48	0.03	106.82	
Overall costs, €						
PO (N = 1,844)	5,834	5,648	0.43	0.03	_	
FUO1 (N = 1,844)	6,253	6,276	0.95	0.00	-208	
FUO2 (N = 1,515)	5,763	5,845	0.86	-0.01	-255	
FUO3 (N = 1,004)	6,038	6,006	0.95	0.00	-150	

Abbreviations: CG, control group; DID, difference-in-differences; FUO, follow-up observation period; IG, intervention group; *N*, number; PO, prior observation period; SMD, standardized mean difference.

Costs

The costs incurred in the outpatient sector were significantly higher for the CorBene participants than the CG across all FUO. Regarding costs in the inpatient sector, there was a nonsignificant cost benefit for the IG across all FUO. Regarding medication costs, no differences could be detected. The overall costs were comparable between IG and CG across all FUO. Observing individual patient changes over time using DID, the costs for CorBene were lower across all FUO. **Table 4** provides an overview of the costs incurred.

Hospital Admissions

The number of hospital admissions is marginally different between the two groups, with fewer admissions for IG across all FUO. In FUO1 (p=0.05) and FUO3 (p=0.08), a slightly

smaller number of hospitalization cases is ascertainable for IG. **Table 5** shows the hospitalization cases for all observation periods.

Indicators of Treatment Quality

Treatment quality comprises the following indicators: number of contacts between patients and their cardiologists, prescription of guideline-driven HF medication, as well as performance of diagnostic procedures, such as echocardiography. The CorBene participants had significantly more contact to their cardiologists across all observation periods (**Fig. 2**).

The proportion of patients with at least one contact to their cardiologist is also significantly higher in the IG across all FUO (FUO1: 89 vs. 75%, p < 0.01; FUO2: 81 vs. 66%, p < 0.01; FUO3:

 Table 5
 Number of hospitalization cases

Parameter	IG	CG	<i>p</i> -Value	SMD	DID	
Number of hospitalization cases						
PO (N = 1,844)	0.80	0.76	0.24	0.0386	-	
FUO1 (N = 1,844)	0.64	0.72	0.05	-0.0640	-0.1220	
FUO2 (N = 1,515)	0.62	0.58	0.41	0.0300	-0.0185	
FUO3 (N = 1,004)	0.54	0.63	0.08	-0.0787	-0.1783	

Abbreviations: CG, control group; DID, difference-in-differences; FUO, follow-up observation period; IG, intervention group; N, number; PO, prior observation period; SMD, standardized mean difference.

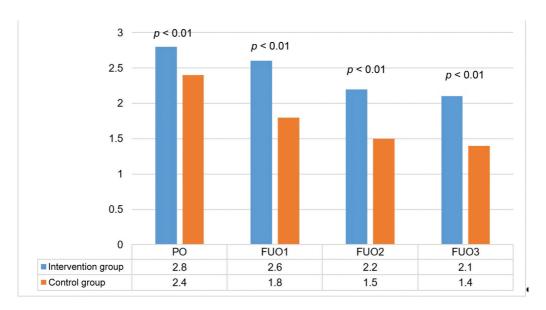


Fig. 2 Mean number of cardiologist contacts. FUO, follow-up observation period.

Table 6 Prescription of heart failure medication

Parameter	IG	CG	<i>p</i> -Value	SMD	DID		
ACE inhibitors, %	ACE inhibitors, %						
PO (N = 1,844)	51.4	51.6	0.92	-0.0033	_		
FUO1 (N = 1,844)	46.9	44.1	0.09	0.0567	0.0298		
FUO2 (N = 1,515)	45.9	42.2	0.04	0.0732	0.0442		
FUO3 (N = 1,004)	44.4	40.1	0.05	0.0868	0.0388		
β-blockers, %							
PO (N = 1,844)	76.7	77.1	0.78	-0.0090	-		
FUO1 (N = 1,844)	75.8	74.9	0.54	0.0201	0.0125		
FUO2 (N = 1,515)	73.5	72	0.37	0.0326	0.0310		
FUO3 (N = 1,004)	72.4	70.9	0.46	0.0332	0.0239		

Abbreviations: CG, control group; DID, difference-in-differences; FUO, follow-up observation period; IG, Intervention group; N, number; PO, prior observation period; SMD, standardized mean difference.

76 vs. 66%, p < 0.01). During the prior observation period (PO), the proportions in IG and CG are identical (p = 1).

Regarding the dosage of ACE inhibitors, no significant difference could be ascertained between the two groups. However, the CorBene participants demonstrated a higher percentage treatment rate with ACE inhibitors, which is significant in FUO2 (**~Table 6**).

There was no difference between the groups regarding performance of echocardiographic examinations during the PO. Across all FUO, however, the percentage was significantly higher in the IG (**Fig. 3**). Overall, the number decreased over time in both the groups.

Mortality

Across all FUO, the mortality rate was lower in the CorBene participants than in the CG. In FUO1 this difference is statistically significant (p = 0.02). In the later observation periods,

differences cease to have statistical significance. **Fig. 4** shows the differences between IG and CG.

Discussion

This study compared CMP participants and nonparticipants with regard to costs, hospital admissions, indicators for treatment quality, and mortality.

Across all FUO, the outpatient costs for CorBene participants were significantly higher (p < 0.01). Since the costs during the PO were similarly high for both groups, this difference seems to be attributable to participation in CorBene and the regular visits to the cardiologist this participation entailed. This seems plausible because specific ambulatory services makeup part of the CorBene program.

No statistically significant differences could be found between the groups for the inpatient sector. Nevertheless, the

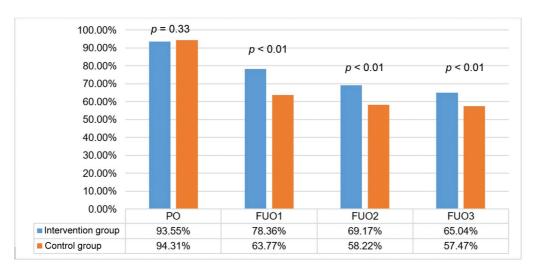


Fig. 3 Performance of echocardiography. FUO, follow-up observation period; PO, prior observation period.

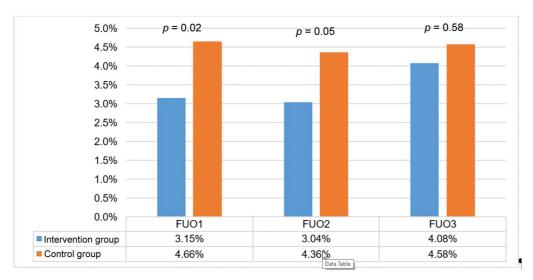


Fig. 4 General mortality. FUO, follow-up observation period.

high negative sums calculated by DID could represent possible inpatient cost benefits for the IG. This supposition is supported by past studies able to demonstrate cost savings in the inpatient sector through ambulatory CMP care. 18,20 Study of the cost-effectiveness of CMP remains controversial, however. 21,22 Against this background, more precise investigations into the cost-effectiveness of CorBene would appear to be beneficial.

There were only slight to no differences in the number of hospitalization cases between IG and CG. During the observation periods FUO1 ($p\!=\!0.05$) and FUO3 ($p\!=\!0.08$), ascertainable differences were not significant. Similar results were observed in the review by Takeda et al.²² Taking the 12 included CMP studies which investigated the inpatient readmission of HF patients during their CMP participation, low to moderate differences between IG and CG could be ascertained. A comparability of the results is conditional,

however, since in these studies the patients were hospitalized and their readmission investigated. In our study, only the number of hospital admissions during the observation period was addressed. This should be investigated in additional studies, especially against the background of the high readmission rate for HF patients.²³

For those individuals with at least one contact to their cardiologist, a benefit for IG could be detected. The demonstrably improved regularity of contact to specialists and more regular diagnostics can, in this context, be interpreted as indicators for improved treatment quality. More frequent consultation of a cardiologist is a guideline-driven recommendation for HF treatment. Here, in particular, the early detection of a deterioration in the clinical picture facilitates a timely introduction of necessary measures.

The frequency of β -blocker prescription was largely identical between the two groups. Only ACE inhibitors tended to

be more frequently prescribed for the CorBene participants. In comparison, a retrospective secondary analysis of routine data throughout Germany by the AOK health insurance company regarding billed medication prescriptions between 2012 and 2013 revealed differences in the administration of the two medications.²⁴ Of the study population examined, 80% were given ACE inhibitors within a year of discharge from hospital, and 63% were given a β-blocker.

The study by Roehl et al was able to show a significantly improved guideline-driven prescription of ACE inhibitors when comparing two groups. 25 One group included patients from routine data of a German health insurance company which encourages increased participation in disease management programs within the context of GP-centered care. In comparison, a standard-care group was investigated. While there were significant differences in the prescription of ACE inhibitors, this was not the case for the administration of β -blockers.

The extent to which CorBene participants are prescribed the recommended dosage of HF medication was not investigated in this study. Taking into account the observed administration of ACE inhibitors and β -blockers below the recommendations for HF patients, ¹² additional studies including the dosage of HF medication are necessary.

The mortality rate in the CorBene group was lower than CG in FUO1 (p=0.02) and FUO2 (p=0.05). The review by Takeda et al included 26 CMP studies which compared mortality rates between IG and CG.²² Their results also suggest that CMP participation could have a lowering effect on mortality rate. The validity of these findings in our context is questionable, however, because not only HF-specific deaths were included. The drawing of conclusions for CorBene participation is therefore impeded.

Limitations

Our study was subject to some limitations, and its validity should therefore be interpreted with caution. Suitable matching partners could only be found for a relatively small proportion of the CorBene population. In particular due to the small number of intervention participants included in the study, generalization of the results is simply not possible. Likewise, the analysis is based on billing data, which means that only information collected in this context is available. It is clear, for example, that individuals were prescribed with certain medications, but unclear whether or not they actually took those medications as prescribed.

It may be assumed that certain selection effects are present which cannot be identified. The results do seem to indicate reduced inpatient costs, but this can also be attributable to chance or selection effects. It is not completely clear from the present database, for example, what reasons physicians have for offering certain patients participation in a program. The offer could be based on existing findings, or individuals with a low hospitalization probability could have been chosen by chance due to the low matching rate.

Mortality should also be interpreted with caution. Here, a selection effect on the part of the physician cannot be

excluded since not all reasons are known for offering a patient participation in a CMP.

Conclusion

CMPs contribute positively to the treatment of HF patients. More frequent contacts between cardiologists and patients, as well as more regular diagnostics, represent an advantage for the CorBene participants. The increased chances of early detection of a deterioration in health could also have a positive impact on treatment quality. Taking the descriptive analysis, there are indications that the IG has an advantage with regard to inpatient costs. In contrast, the outpatient costs of the program participants are higher. The evaluation contained a wide range of variables which need to be focused on more specifically in future studies.

Against the background of frequent hospitalizations due to the high decompensation risk with HF, discharge management must be structured to guarantee continual care, as well as optimize communication between patients, next of kin, GPs, and specialists. Signs of decompensation, for example, can then be detected early and corresponding treatments begun.

One example of comprehensive integration and realization of such an HF network is the Kölner Herzen Atmen Durch (KHAD) model in the Cologne region. ²⁶ It seeks to improve the information and communication paths between individual HF units at different care levels. Through the implementation of such integrated care models for HF patients, standards and quality characteristics for inpatient and follow-up ambulatory care, as well as the transition between the two, can be defined and evaluated. Interaction between different service providers within the KHAD model has the potential to improve quality of care for HF patients considerably, as well as to reduce the costs to the health care system. The effectivity of the HF network remains to be assessed.

Ethical Approval

Ethical approval for this study was waived by the Ethics committee of the University Witten/Herdecke.

Availability of Data and Material

Statistical evaluations were performed by the Institute for Applied Health Research Berlin GmbH—InGef. An allowance was paid for data fusion and statistical evaluations. InGef is a subsidiary of spectrumK GmbH, which belongs to the Association of Professional and Guild Health Insurance Companies. Together with BNK Service GmbH—a subsidiary of the Professional Association of Cardiologists in Private Practice—spectrumK is one of the CorBene frame contract partners and responsible for participant management and billing control for the health insurance companies. Some of the health insurance companies participating in the evaluation are partners in the spectrumK GmbH company. The data underlying this article will be shared on reasonable request to the corresponding author.

Authors' Contributions

J.E., H.J.N., and P.M.B. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. He discussed the results and contributed to the final manuscript. D.G. provided critical feedback and helped shape the research, analysis, and manuscript. M.M., F.G., W.H., and S.G. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

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Conflict of Interest

None declared.

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