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Abkürzungsverzeichnis

AOK:	Allgemeine Ortskrankenkasse
CAD:	Koronare Herzkrankheit
CHF:	Chronic Heart Failure, Chronische Herzinsuffizienz
CI:	Konfidenzintervall
DRG:	Diagnosis Related Groups, Diagnosebezogene Fallgruppen
ICER:	Incremental cost-effectiveness ratio
Morbi-RSA:	Morbiditätsorientierter Risikostrukturausgleich
NYHA:	New York Heart Association
QALY:	Quality-Adjusted Life Year
RCT:	Randomised controlled trial, randomisierte klinische Studie
RR:	Relatives Risiko
T2D:	Typ-2-Diabetes

1 Einleitung

Das Bundesgesundheitsblatt berichtete im Oktober 2015 in einem Schwerpunkttheft über den Stand und die Perspektiven der Telemedizin in Deutschland [1]. Vielfach bestehen telemedizinische Anwendungen aus regionalen Lösungen, obwohl sich Verteilung und Versorgungssituation bei chronischen Erkrankungen bundesweit nicht grundsätzlich unterscheiden [2]. Als großes Hindernis für die flächendeckende Umsetzung telemedizinischer Anwendungen erweist sich der langwierige und teure Evidenznachweis mittels klinischer Studien. Brauns und Loos plädieren für eine methodische Flexibilisierung bei der Evaluation telemedizinischer Programme [3]. Hier setzt die vorliegende Dissertation mit der Evaluation eines telemedizinischen Interventionsprogrammes für Herzinsuffizienzpatienten in der Versorgungsrealität an. In der Analyse werden methodische Aspekte der Datengrundlage und des Studiendesigns besprochen sowie der Nutzen des Programmes für die Patientinnen und Patienten (hier in erster Linie: Überlebensdauer) und für die Träger der gesetzlichen Krankenversicherung (Gesundheitskosten) untersucht.

1.1 Einteilung, Therapie und Epidemiologie der Herzinsuffizienz

Herzinsuffizienz bezeichnet die krankhafte Unfähigkeit des Herzens, den Organismus mit ausreichend Blut und Sauerstoff zu versorgen, um den Stoffwechsel zu gewährleisten. Nach dem Schema der New York Heart Association (NYHA) wird die Schwere der Erkrankung in die Stadien NYHA I („ohne körperliche Limitation“) bis NYHA IV („Beschwerden bei allen körperlichen Aktivitäten und in Ruhe“) eingeteilt. Weitere Einteilungen existieren hinsichtlich des Verlaufs (akut, chronisch), der überwiegend betroffenen Herzhälften (links, rechts, global) und des hämodynamischen Mechanismus (Vorwärts-, Rückwärtsversagen) der Erkrankung. Die Behandlung chronischer Herzinsuffizienz (CHF) umfasst die Bereiche Kontrolle und Therapie von Prognosefaktoren, kausale Therapie der verursachenden Erkrankung, nicht-medikamentöse Therapie (u.a. Modifikation des Lebensstils, körperliches Training, Gewichtskontrolle), medikamentöse Therapie, operative und apparative Therapie, Rehabilitation und palliative Therapie. Behandlungsziele der Therapiemaßnahmen sind u.a. Senkung der

Sterblichkeit, Senkung der Anzahl von Notarzteinsätzen und Krankenhausaufnahmen und die Verbesserung der Lebensqualität [4].

Die durchschnittliche internationale Prävalenz von CHF beträgt 3 bis 20 Fälle je 1 000 Personen. Die Prävalenz ist stark vom Alter abhängig, in der Altersgruppe ab 65 Jahren liegt sie bei über 100 Fällen je 1 000 Personen. In den jüngeren Altersklassen sind eher Männer, in den höheren Altersklassen eher Frauen betroffen [5]. Herzinsuffiziente Patientinnen und Patienten verursachen in Deutschland 2,3-fach höhere durchschnittliche Kosten im ambulanten Bereich pro Versicherten (778 Euro gegenüber 340 Euro bei allen Krankenversicherten). Auch die Kosten für Arzneimittel sind in der Gruppe der Menschen mit Herzinsuffizienz deutlich erhöht (1 073 Euro gegenüber 366 Euro bei allen Krankenversicherten) [6]. Bei vollstationären Fällen in Deutschland steht die Diagnose Herzinsuffizienz an dritter Stelle bei Männern und ist bei Frauen die häufigste Diagnose. Als vierthäufigste Todesursache unter Männern und zweithäufigste bei Frauen bildet Herzinsuffizienz einen Hauptgrund für Mortalität in Deutschland [7]. Goldberg et al. geben eine durchschnittliche 5-Jahres-Sterblichkeit von 62,5% an [8].

1.2 Telemedizinische Interventionsprogramme

Die Fernversorgung mit Gesundheitsdiensten und klinischen Informationen mittels Telekommunikationstechnologie („remote delivery of health care services and clinical information using telecommunications technology“) wird nach Definition der American Telemedicine Association (AFA) als Telemedizin bezeichnet. In der Regel werden die Begriffe „Telemedizin“ (telemedicine) und „Telegesundheit“ (telehealth) synonym verwendet [9]. Telemedizinische Anwendungen existieren aktuell in drei Formen: Telekonsile zum interdisziplinären Austausch zwischen ärztlichen Kolleginnen und Kollegen („doc2doc“), Telemonitoring zum kontinuierlichen Monitoring von Vitalparametern und Teletherapie („doc2patient“) [1].

Innovative Versorgungskonzepte mit telemedizinischen Komponenten haben das Potenzial, die medizinische Versorgung zu unterstützen und Lücken in der flächendeckenden Versorgung insbesondere in ländlichen Regionen zu überbrücken [10]. Die Deutsche Gesellschaft für Kardiologie empfiehlt, dass Patientinnen und Patienten mit Herzinsuffizienz in ein multi-

disziplinäres Managementprogramm aufgenommen werden, um das Risiko für Krankenhausaufnahmen zu reduzieren [11].

In einem Cochrane Review (systematische Übersichtsarbeit) betrachten Inglis et al. insgesamt 41 Studien zur strukturierten telefonischen Unterstützung (25 Studien) bzw. zum nicht-invasiven Telemonitoring (18 Studien) für Menschen mit Herzinsuffizienz und zeigen die grundsätzliche Wirksamkeit der Programme bei der Reduktion der Gesamtmortalität, der CHF-bedingten Krankenhausaufenthalte und der Gesundheitskosten [12].

1.3 Routinedaten in der Gesundheitsversorgung

Randomisierte klinische Studien (randomised controlled trial, RCT) bilden in der evidenzbasierten Medizin die Grundlage für den empirischen Nachweis der Wirksamkeit von Behandlungen. Es ist aber nicht immer möglich und nötig, (telemedizinische) Anwendungen im Gesundheitswesen in RCTs zu evaluieren [13]. Bei neuen Versorgungsmodellen liegt häufig ein nicht-randomisiertes Untersuchungsdesign zugrunde. Aus den Sekundärdaten kann retrospektiv eine Vergleichsgruppe gebildet werden, die sich nicht systematisch von der Interventionsgruppe unterscheidet [14].

Die Analyse auf Basis von Routinedaten hat gegenüber einer kostenintensiven randomisierten Studie die Vorteile des Einschlusses einer breiten Population, also einer größeren Repräsentativität des Versorgungsgeschehens. Durch die Struktur der Daten können sowohl Quer- als auch Längsschnittanalysen durchgeführt werden. Da die so durchgeführten Gesundheitskostenanalysen auf Abrechnungsdaten basieren, besitzen die Ergebnisse eine hohe praktische Relevanz für die Krankenkasse. Eine Einschränkung erfahren solche Studien durch die Abhängigkeit von der Kodierqualität der Daten und der Tatsache, dass Routinedaten für Abrechnungszwecke erhoben werden und damit in erster Linie Variablen abbilden, die abrechnungsrelevant sind. Diagnosen in Routinedaten enthalten Verdachts- und Ausschlussdiagnosen und können verzerrt sein, beispielweise in Folge von Upcoding (Angabe von höherem Schweregrad) im Rahmen des Risikostrukturausgleiches (Morbi-RSA) oder im DRG-System (Diagnosebezogene Fallgruppen, Diagnosis Related Groups) [15].

2 Material und Methoden

2.1 Datengrundlage

Das Programm *Cordiva* innerhalb des Herzinsuffizienzprogramms *AOK-Curaplan Herz Plus* (AOK Nordost, Allgemeine Ortskrankenkasse für Berlin, Brandenburg und Mecklenburg-Vorpommern) richtet sich an Versicherte mit einem hohen Risiko für einen Krankenhausaufenthalt aufgrund der Indikation Herzinsuffizienz [16]. Details zum Interventionsprogramm, der Rekrutierung von Interventionspatientinnen und -patienten und dem Studiendesign sind in [17] und [18] beschrieben. In die Analyse gingen alle Versicherten ein, die zwischen dem vierten Quartal 2006 und dem zweiten Quartal 2012 in das Programm aufgenommen wurden.

Die Rohdaten bestanden aus 13 Datensätzen aus dem Datenbestand der AOK Nordost. Das Datenmodell (Tab. 1) zeigt die Herkunft der Datensätze aus den Bereichen Grunddaten der Versicherten, Programminformationen zu den Teilnehmerinnen und Teilnehmern, Gesundheitskosten und Kostenklassen, Medikation, Psychische Erkrankungen („F-Diagnosen nach ICD-10“), Angaben zu stationären und ambulanten Leistungen.

Die Verknüpfung der Datensätze erfolgte anhand von projektspezifischen eindeutigen Bezeichnungen zur Identifikation der Versicherten (ID-Nummern). Neben der Plausibilitätskontrolle der Angaben war eine umfangreiche Datenvorbereitung notwendig, da die Struktur der Datensätze nicht einheitlich war. Bei einigen Parametern lagen die Angaben quartalsweise vor, z.B. die Höhe der (gesamten) Gesundheitskosten für jeden Versicherten in jedem Quartal ab dem Beginn des Jahres 2006. Bei vielen weiteren Variablen lagen die Angaben nur vor, wenn ein Fall (z.B. eine Krankenhausaufnahme, eine ambulante Behandlung oder Medikation mit einem Wirkstoff) tatsächlich eingetreten ist. Diese Daten wurden in die quartalsweise Struktur (z.B. Summe der Krankenhausaufnahmen pro Quartal) umgewandelt. Der Algorithmus zur Ermittlung des NYHA-Stadiums in jedem Quartal wird im Folgenden beschrieben und es werden weitere wesentliche Variablen erläutert.

2 Material und Methoden

Tabelle 1: Datenmodell der Rohdaten

Name des Datensatzes	Inhalt	Anzahl der Variablen
EXP_D_67_10_VERS_INFO_HI_PAT	Angaben zur Person	15
EXP_D_67_12_TEILN_CORDIVA_INFO	Angaben zu den Versicherten im Programm	7
EXP_D_67_14_KOSTENKLASSEN	Kostenklassen je Quartal	3
EXP_STG_67_32_NYHA_AMB_KH_VERS	NYHA-Stadium und indikationsbezogene Krankenhausaufenthalte	7
EXP_STG_67_38_F_DIAGS_JE_QUART	F-Diagnosen	6
EXP_STG_67_39_KST_JE_QUART	Krankheitskosten je Quartal	13
EXP_STG_67_40_ATC_F_DIAGS_PVT	Medikation und weitere quartalsweise Angaben	27
EXP_STG_67_52_KH_FAELLE	Stationäre Krankenhausfälle (ohne Reha)	16
EXP_STG_67_54_KH_DIAGNOSEN	Diagnosen zu den KH-Fällen	6
EXP_STG_67_56_KH_OPD	Operationsschlüssel (OPS) zu den KH-Fällen	8
EXP_STG_67_60_AMB_FAELLE	Ambulante Behandlungsfälle	6
EXP_STG_67_62_AMB_LEISTUNG	Gebührenordnungsnummern (GONR) zu den ambulanten Behandlungsfällen	7
EXP_STG_67_64_AMB_DIAGNOSEN	Diagnosen zu den ambulanten Behandlungsfällen	6

NYHA-Stadium: Das NYHA-Stadium wurde im Rahmen von stationären und ambulanten Behandlungen ermittelt. Im Datensatz lag somit nicht für jedes Quartal ein NYHA-Stadium je Person vor, in anderen Quartalen jedoch mehrere, teils unterschiedliche NYHA-Stadien bei einer Person. Ein Algorithmus ermittelte aus diesen Rohdaten für jedes Quartal ein NYHA-Stadium pro Person unter der Annahme, dass ein NYHA-Stadium solange gültig bleibt, bis das nächste erhoben wird. Wenn für ein Quartal mehr als ein NYHA-Stadium vorlag, wurde

in einer ersten Priorisierung ein stationär gemessenes NYHA-Stadium höher als ein ambulantes und, in einer zweiten Priorisierung, ein höheres höher als ein niedrigeres NYHA-Stadium gewichtet. Der Algorithmus arbeitete ausschließlich prospektiv, d.h. das ermittelte NYHA-Stadium war für das aktuelle und alle folgenden Quartale gültig bis ein neues NYHA-Stadium aus den Daten hervorgeht. Ein ermitteltes NYHA-Stadium wurde aber nicht auf vorhergehende Quartale übertragen.

Herzinsuffizienzbezogene Krankenhausaufnahmen: Eine herzinsuffizienzbezogene Krankenaufnahme wurde definiert als ein Krankenaufenthalt, bei dem ein NYHA-Stadium dokumentiert wurde.

Kosten und Kostenklassen: Die Kostenklasse wurde auf Basis des Quartalsdurchschnitts der Gesamtkosten eines Versicherten in den 3 Quartalen vor Einschluss und dem Einschlussquartal berechnet. Die Klassenbildung folgte der AOK-Klasseneinteilung und reichte von Klasse 0 (negative Werte) bis Klasse 22 (> 30 000 Euro). Die Klassen hatten unterschiedliche Klassenbreiten. Um den großen Einfluss der Hochkostenfälle zu begrenzen, wurde in den Untersuchungen der Gesamtkosten das kombinierte Ausschluss- und Kappungsverfahren der AOK Nordost angewendet:

1. Versicherte, die innerhalb eines Jahres Gesamtkosten von 100 000 Euro verursachten, wurden aus der Analyse der Gesamtkosten ausgeschlossen. Es ist anzunehmen, dass die hohen Kosten in vielen Fällen durch ein einmaliges Ereignis (z.B. Unfall) entstanden und nicht im Zusammenhang mit der Herzinsuffizienz stehen. Auch die gematchten Fälle dieser Hochkostenfälle wurden aus der Analyse ausgeschlossen.
2. Krankenhauskosten von mehr als 20 000 Euro pro Jahr, Kosten für häusliche Krankenpflege über 15 000 Euro pro Jahr und Arzneimittelkosten über 7 000 Euro pro Jahr wurden bei der Berechnung der Gesamtkosten als Summe der Kostensektoren bei 20 000 Euro, 15 000 Euro bzw. 7 000 Euro gekappt.

Medikation: Die betrachteten Wirkstoffe waren ACE-Hemmer (C09 A), Beta-Rezeptorenblocker (C07A), Renin-Inhibitoren (C09X), Herzglykoside (C01A), Diuretika (C03A, C03B, C03C, C03D, C03E) und AT1-Rezeptorenblocker (C09C, C09D).

Wohnregion: Die Variable lag nur für den Zeitpunkt der Datenbankabfrage vor und ist deshalb kein Matchingkriterium.

Versicherungsende: Versicherte konnten nur in einem Quartal gematcht werden und damit in die Studienpopulation eingehen, wenn sie im gesamten Quartal bei der AOK Nordost versichert waren. Bei den Untersuchungen der jeweiligen Endpunkte wurden nur Personen berücksichtigt, die im gesamten Follow-up-Zeitraum (in der Regel 1 oder 2 Jahre nach Aufnahme / Baseline) versichert waren.

Sterbedatum / Überleben: Versicherte galten in der Analyse als „verstorben innerhalb eines Jahres“, wenn das Sterbedatum in den vier Quartalen nach Einschluss lag (analog beim 2-Jahres-Überleben).

2.2 Propensity-Score Matching

Während die Idee des Propensity-Score Matchings bereits in den 1970er Jahren entwickelt wurde [19], gehören Matchingverfahren erst seit wenigen Jahren zu den Routineverfahren der Sekundärdatenanalyse [20]. Der Propensity-Score ist die Wahrscheinlichkeit, dass eine Einheit (z.B. eine Person) mit ihrer Kombination von Kovariaten einer bestimmten Behandlung zugeordnet wird [21]. Das Propensity-Score Matching umfasst das Durchführen einer logistischen Regression, Kontrolle des berechneten Scores innerhalb der Gruppen, Zuordnung von Teilnehmenden und Nicht-Teilnehmenden, Kontrolle der Balance der (gewichteten) Kovariaten zwischen den Gruppen und das Durchführen geeigneter multivariater Verfahren.

Im Software-Paket „MatchIt“ für R sind die Propensity-Score Verfahren „Exact matching“, „Subclassification“, „Nearest neighbor matching“ (ein Greedy-Algorithmus), „Optimal matching“ (Algorithmus: RELAX-IV minimum cost flow solver), „Full matching“ und „Genetic matching“ (ein genetischer Suchalgorithmus zur Gewichtung der Variablen) implementiert [22]. Durch die kontinuierliche Einstufung der Interventionspatientinnen und -patienten über 23 Quartale (Q4 2006 bis Q2 2012) wurden im Algorithmus 23 quartalsweise Matching-durchläufe mit einem Recycling der noch nicht gematchten „Usual-care Gruppe“ durchgeführt. Die Auswahl der Matchingvariablen folgte theoretischen Überlegungen. In der Analyse wurden drei Verfahren verglichen: das Matchingverfahren der Publikationen (Kombination

aus Nearest-neighbor Matching und exaktem Matching), ein Nearest-neighbor Matching ohne exaktes Matching und Optimal Matching anstelle des Nearest-neighbor Matching.

2.3 Statistische Analyse

Der Vergleich der Matchingverfahren wurde mithilfe von deskriptiven Analysen und ungepaarten t-Tests sowie Chi-Quadrat-Tests durchgeführt. Zusätzlich wurde die Laufzeit der Algorithmen zum Matching ermittelt. Die Programme wurden auf einem Intel® Core i7 Prozessor mit 2,9 GHz und 8 GB RAM unter macOS Mojave ausgeführt.

Die Hauptergebnisse im Abschnitt „Überleben und Krankenhausaufnahmen“ wurden in binär-logistischen (Überleben) bzw. Negativ-Binomial-Regressionsmodellen (Krankhausaufnahmen) berechnet. In der vorliegenden Untersuchung wurde der, bereits in der Publikation diskutierte, Ansatz der Survival-Analyse durch Auswertung der Kaplan-Meier-Schätzer und einer Cox-Regression näher spezifiziert. Die Proportional Hazard Assumption des Models wurde mit Schönfeld-Residuen getestet. In allen Analysen wurde ein p-Wert < 0,05 als statistisch signifikant definiert.

Das Regressionsmodell der Gesundheitskosten wurde für alle Matchingvariablen und die Wohnregion adjustiert. Die Interaktion „Studiengruppe x Wohnregion“ wurde in das Modell aufgenommen, da bivariate Analysen eine Auswirkung einer Änderung der Intervention des Wohnortes auf die gesamten Gesundheitskosten zeigten. Die graphische Darstellung des Interaktionseffekts erfolgte mithilfe der „marginal effects“ (marginale Effekte, auch Grenzefekte) des Regressionsmodells. Diese zeigen, wie sich eine abhängige Variable (hier: Gesundheitskosten) ändert, wenn sich bestimmte unabhängige Variablen (hier: Studiengruppe und Wohnregion) ändern. Alle anderen unabhängigen Variablen wurden konstant gehalten.

Die Analysen in den Publikationen wurden mit der Statistiksoftware R, Version 3.0.0 durchgeführt, die zusätzlichen Berechnungen basierten auf der R-Version 3.5.0 [23]. Sofern nicht anders angegeben, sind die verwendeten Prozeduren in den Paketen „base“ und „stats“ implementiert. Außerdem wurden die Pakete „MatchIt“ [22] für das Matching, „survey“ [24] für gewichtete Analysen, „survival“ [25] und „survminer“ [26] für Survival-Analysen sowie „ggplot2“ [27] und „ggeffects“ [28] für die Visualisierung verwendet.

3 Ergebnisse

3.1 Datenvorbereitung und Matching

Der Analysedatensatz aus dem Datenbestand der AOK Nordost enthielt Informationen zu 2 622 Versicherten, die im Zeitraum vom 4. Quartal 2006 bis zum 2. Quartal 2012 in das Programm *Cordiva* aufgenommen wurden. Die Grundlage der Kontrollgruppe bildeten 205 738 Versicherte der AOK Nordost, die ebenfalls die Einschlusskriterien für das *Cordiva*-Programm erfüllten, jedoch nicht am Programm teilgenommen hatten.

Das gewählte Propensity-Score Matchingverfahren bestand aus der Kombination der Nearest-neighbor Methodik mit exaktem Matching in ausgewählten Variablen. Insgesamt 5 662 gematchte Fälle wurden in die Analyse eingeschlossen (davon 1 943 mit Intervention, 3 719 Fälle ohne Intervention). Im Verhältnis 1:2 konnten 1 776 Interventionspatientinnen und -patienten gematcht werden, für 167 Interventionsfälle existierte jeweils nur ein Kontrollfall.

Tabelle 2 zeigt die Ergebnisse der Gruppen (Telemedizin bzw. Kontrollgruppe) in ausgewählten Variablen zur Baseline. Die Übersicht zeigt u.a. Variablen, die als Matchingparameter (exakt bzw. Propensity-Score) dienen. Weiterhin sind Variablen aufgeführt, die nicht oder nur indirekt über andere Parameter (z.B. Gesundheitskosten und Kostenklassen) gematcht werden.

Die Gruppen zeigten eine gute Übereinstimmung (mit Ausnahme der Anzahl der Notarzteinsätze). In der Publikation zum Überleben wurde außerdem gezeigt, dass die gematchte ($N = 1\,943$) und die gesamte Telemedizingruppe ($N = 2\,622$) gut übereinstimmen.

3 Ergebnisse

Tabelle 2: Ausgewählte Baseline-Charakteristika der gematchten Versicherten

Variable		Telemed.-Gr. gesamt (N = 2 622)	Nearest Neighbor + Exaktes Matching			Nearest Neighbor		
			Telemedizin (N = 1 943)	Kontrollgr. (N = 3 719)	p-Wert	Telemedizin (N = 2 571)	Kontrollgr. (N = 5 142)	p-Wert
Geschlecht	Männer	1 439 (54,88%)	1 052 (54,14%)	2 014 (54,15%)	-	1 401 (54,49%)	2 714 (52,78%)	0,163
	Frauen	1 183 (45,12%)	891 (45,86%)	1 705 (45,85%)		1 170 (45,51%)	2 428 (47,22%)	
NYHA-Stadium	NYHA I - III	1 584 (71,74%)	1 412 (72,67%)	2 702 (72,67%)	-	1 569 (72,17%)	2 776 (64,13%)	< 0,001
	NYHA IV	624 (28,26%)	531 (27,33%)	1,16 (27,33%)		605 (27,83%)	1 553 (35,87%)	
	Missing	414	-	-		397	813	
Medikation	Beta-Blocker	1 643 (63,05%)	1 261 (64,90%)	2 340 (62,93%)	0,152	1 630 (63,40%)	3 386 (65,85%)	0,036
	Diuretika	1 643 (63,05%)	1 298 (66,80%)	2 507 (67,40%)	0,673	1 622 (63,09%)	3 348 (65,11%)	0,085
Alter [Jahre]		73,73 (SD: 9,64)	74,44 (SD: 8,97)	74,48 (SD: 9,04)	0,900	73,69 (SD: 9,64)	73,80 (SD: 10,83)	0,647
Gesundheitskosten [Euro pro Quartal]		3 918,40 (SD: 3 904,32)	3 746,80 (SD: 3 007,20)	3 750,10 (SD: 3 021,40)	0,971	3 875,80 (SD: 3 877,80)	4 432,40 (SD: 5 737,30)	< 0,001
Notarzteinsätze pro Jahr		0,64 (SD: 1,27)	0,65 (SD: 1,27)	0,55 (SD: 1,30)	0,006	0,63 (SD: 1,26)	0,52 (SD: 1,20)	< 0,001
Laufzeit des Algorithmus		-	58:02 Minuten			7:21 Minuten		

Grüner Hintergrund: Exaktes Matching der Variable, Gelb: Propensity-Score Matching,

Orange: „Indirektes Matching“ (exaktes Matching von Altersgruppen und Kostenklassen), Rot: Keine Matching-Variable

Hervorgehobener p-Wert: signifikanter Unterschied zwischen Interventions- und Kontrollgruppe

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Falls auf die exakte Übereinstimmung verzichtet wird und die Ähnlichkeit der Gruppen nur mittels Propensity-Score Matching erzielt werden soll, konnte eine größere Anzahl an Interventionspatientinnen und -patienten ($N = 2\,571$) gematcht werden. Gründe für das Nicht-Matching von 51 Versicherten in diesem Verfahren waren die Aufnahme in das Programm im ersten und zweiten Quartal 2012, hierfür lagen nur Personalgrunddaten, aber keine Abrechnungsdaten vor ($N = 16$). Der zweite Grund für das Scheitern des Matching war eine zu große Distanz im Propensity-Score ($N = 35$). Die Übereinstimmung nach diesem Verfahren war schlechter, es gibt zwischen den Gruppen signifikante Unterschiede im NYHA-Stadium, im Alter, in den Gesundheitskosten pro Quartal im Jahr vor Einschluss und in der Anzahl der Notarzteinsätze.

Optimal Matching ist eine Abwandlung des Nearest-neighbor Verfahrens und erzielte im Wesentlichen ähnliche Ergebnisse wie das Nearest-neighbor Matching. Allerdings war der Algorithmus mit einer Laufzeit von 72 Minuten langsamer als die anderen beiden Verfahren.

Unter diesen Voraussetzungen wurde ein kombiniertes Verfahren aus Propensity-Score Matching (Nearest-neighbor) und exaktem Matching zur Bestimmung von Interventions- und Kontrollgruppe gewählt.

3.2 Überleben und Krankenhausaufnahmen

Die Hauptergebnisse der veröffentlichten Studie waren eine höhere Überlebenswahrscheinlichkeiten der Versicherten der Telemedizingruppe im Vergleich zur Kontrollgruppe nach einem Jahr (adjustiertes OR: 1,47, 95%-CI: 1,21 - 1,80, $p < 0,001$) und zwei Jahren (adjustiertes OR: 1,51, 95%-CI: 1,28 - 1,77, $p < 0,001$). Die Überlebenschancen nach einem Jahr waren für die weibliche Telemedizingruppe im Vergleich zur Kontrollgruppe (OR = 1,75, 95%-CI: 1,29 - 2,38) stärker erhöht als für die männliche Telemedizingruppe (OR = 1,26, 95%-CI: 0,97 - 1,65).

In Tabelle 3 ist die Entwicklung der Gruppengrößen der Telemedizingruppe („Personen unter Risiko“) pro Quartal im Zeitverlauf dargestellt (mit Baseline = Quartal 0). Weiterhin wird dort die Anzahl der verstorbenen Personen und die Anzahl der zensierten Fälle (Wechsel der Krankenversicherung oder Ende des Follow-up-Zeitraums nach Q2 2012) gezeigt. Auffällig ist

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die große Zahl der zensierten Fälle nach dem neunten und zehnten Quartal. Diese ist dadurch begründet, dass der Großteil der Versicherten im vierten Quartal 2009 und ersten Quartal 2010 in das Programm aufgenommen wurde und diese nach dem zweiten Quartal 2012 das Ende des Follow-up-Zeitraumes erreichten. Die Überlebenswahrscheinlichkeit der Telemedizingruppe betrug 89,1% nach einem, 79,4% nach zwei und 68,8% nach drei Jahren. Methodisch bedingt sind geringfügige Abweichungen zur Publikation zu beobachten.

Tabelle 3: Survival-Analyse mit Kaplan-Meier-Schätzer in der Telemedizingruppe

Quartale nach Baseline	Personen unter Risiko	Todes- fälle	Zensierte Fälle*	Kaplan- Meier- Schätzer	95%-CI	
					2,5%	97,5%
0	1 943	-	1	100,0%	100,0%	100,0%
1	1 942	58	2	97,0%	96,3%	97,8%
2	1 882	48	8	94,5%	93,5%	95,6%
3	1 826	57	13	91,6%	90,4%	92,8%
4	1 756	48	11	89,1%	87,7%	90,5%
5	1 697	57	14	86,1%	84,6%	87,7%
6	1 626	38	17	84,1%	82,5%	85,7%
7	1 571	38	35	82,0%	80,3%	83,8%
8	1 498	49	145	79,4%	77,6%	81,2%
9	1 304	43	719	76,7%	74,8%	78,7%
10	542	22	355	73,6%	71,4%	75,9%
11	165	2	21	72,7%	70,2%	75,3%
12	142	8	11	68,6%	65,1%	72,4%

* Wechsel der Krankenversicherung oder Ende des Follow-up-Zeitraums erreicht

Die graphische Darstellung verdeutlicht, dass die Überlebenswahrscheinlichkeit der Versicherten der Telemedizingruppe im Vergleich zur Kontrollgruppe in den ersten drei Jahren höher ist (Abb. 1). Unter deutlich rückläufiger Zahl der Personen unter Risiko glichen sich die Überlebenswahrscheinlichkeiten ab Mitte des dritten Jahres an. Die Gruppen unterschieden

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sich in der kumulierten Überlebenswahrscheinlichkeit mit $p < 0,001$ (Log Rank Test) signifikant.

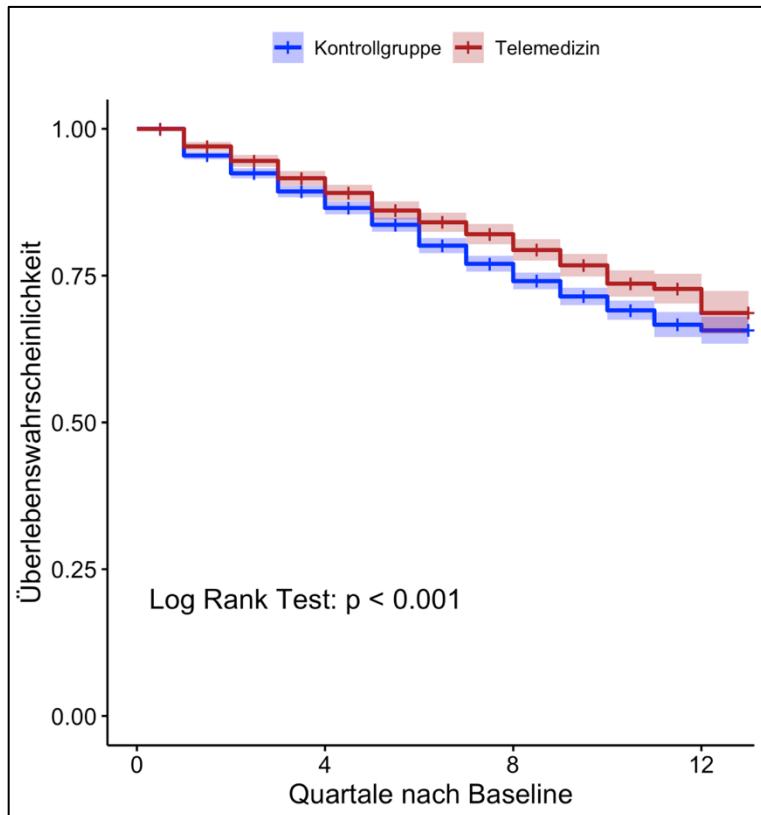


Abbildung 1: Überlebenswahrscheinlichkeit in den drei Jahren nach Baseline

Der gleichzeitige Einfluss von mehreren Variablen auf das Überleben wird in Tabelle 4 dargestellt. Der Test der Schoenfeld-Residuen zeigte, dass die Proportional Hazard Assumption nicht verletzt war ($p = 0,071$ für das gesamte Modell). Bereits in der Publikation wurde diskutiert, dass die Intervention einen signifikanten positiven Einfluss ($HR = 0,78$, 95%-CI: $0,69 - 0,88$, $p < 0,001$) auf das Überleben hatte. Weitere Variablen mit einem signifikanten positiven Einfluss waren das weibliche Geschlecht, das NYHA-Stadium (hier aber nur NYHA II vs. NYHA I) sowie die Einnahme von ACE-Hemmern, Beta-Rezeptorenblockern oder AT1-Rezeptorenblockern. Ein signifikanter negativer Einfluss auf das Überleben ging von höherem Alter, mehr CHF-bezogenen Krankenhausaufnahmen im Jahr vor Baseline, höheren Gesundheitskosten sowie der Einnahme der Wirkstoffe Herzglykoside und Diuretika aus.

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Tabelle 4: Cox-Regression der Überlebenszeiten (N = 5662)

Variable*	Referenz	Hazard Ratio	95%-CI		p-Wert
			2,5%	97,5%	
Gruppe: Telemedizin vs. KG	Kontrollgruppe	0,78	0,69	0,88	< 0,001
Region: Berlin vs. Nicht-Berlin	Nicht-Berlin	1,12	1,00	1,26	0,054
Alter [Jahre]	(kont.)	1,05	1,04	1,05	< 0,001
Geschlecht	Männlich	0,83	0,75	0,93	0,001
NYHA-Stadium					
- NYHA II	NYHA I	0,58	0,36	0,93	0,024
- NYHA III	NYHA I	0,71	0,45	1,14	0,161
- NYHA IV	NYHA I	0,92	0,57	1,47	0,718
CHF-bezogene KH-Aufnahmen	(kont.)	1,14	1,08	1,21	< 0,001
Gesamtkosten [1 000 € / Quartal]	(kont.)	1,06	1,05	1,08	< 0,001
Medikation					
- ACE-Hemmer	nein	0,87	0,78	0,97	0,009
- Beta-Rezeptorenblocker	nein	0,78	0,71	0,87	< 0,001
- Renin-Inhibitoren	nein	0,82	0,52	1,30	0,400
- Herzglykoside	nein	1,30	1,14	1,48	< 0,001
- Diuretika	nein	1,49	1,32	1,68	< 0,001
- AT1-Rezeptorenblocker	nein	0,73	0,63	0,84	< 0,001

* Modell zusätzlich adjustiert für psychische und Verhaltensstörungen

Als sekundärer Endpunkt wurde die Anzahl der Krankenhausaufnahmen untersucht. Die durchschnittliche Anzahl der gesamten Krankenhauseinweisungen pro Jahr betrug 1,56 für die Telemedizingruppe und 1,57 für die Kontrollgruppe im ersten Jahr. Im Vergleich zur Baseline (2,54 bzw. 2,53 pro Jahr) zeigte sich in beiden Gruppen ein Rückgang. Die Anzahl der CHF-bezogenen Krankenhausaufnahmen beider Gruppen betrug 0,61 pro Jahr, auch dies war eine Reduzierung gegenüber dem Basiswert von 1,37 für beide Gruppen.

3.3 Gesundheitskosten

Die Hauptanalyse der Publikation zu den Gesundheitskosten zeigte eine Interaktion zwischen der Intervention und der Wohnregion der Versicherten. Die Gesundheitskosten der Telemedizingruppe im Vergleich zur Kontrollgruppe waren nach 12 Monaten bei den Teilnehmern mit Wohnort Berlin um 18€ pro Quartal und in den anderen Regionen um 276€ pro Quartal niedriger. In der Darstellung des gemeinsamen Einflusses von Studiengruppe und Wohnregion auf die Gesundheitskosten (Abb. 2) sind alle Variablen bis auf die Intervention und die Wohnregion auf den Mittelwert (bei kontinuierlichen Variablen) bzw. die Referenzkategorie fixiert, die Grafik bildet also die zu erwartenden Gesundheitskosten für einen durchschnittlichen Versicherten der jeweiligen Gruppen ab. Der gemeinsame Einfluss von Intervention und Wohnregion zeigt sich hier durch die Unterschiede im Mittelwert der Gesundheitskosten. Die Standardfehler verdeutlichen eine große Varianz in der Datenlage.

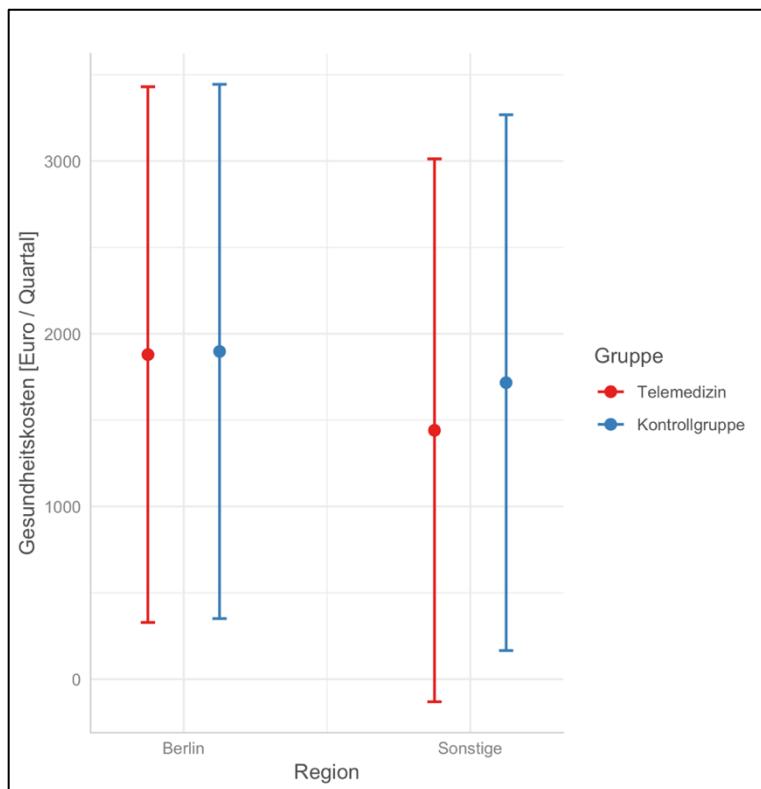


Abbildung 2: Durchschnittliche Gesundheitskosten pro Person und Quartal nach einem Jahr

4 Diskussion

Im Rahmen der vorliegenden Analyse wurde auf der Basis von Abrechnungsdaten das Programm *Cordiva* der AOK Nordost evaluiert. Dass die Intervention in der Routineversorgung durchgeführt wurde und anfangs keine Evaluation des Programms vorgesehen war, musste beim Evaluationsdesign berücksichtigt werden.

Auswahl des Matchingverfahrens

Ein kombiniertes Verfahren aus Propensity-Score Matching und exaktem Matching zur Bestimmung von Interventions- und Kontrollgruppe erwies sich als am besten geeignet. Dies wurde anhand der resultierenden Gruppengröße und der Ähnlichkeit der Interventions- und Kontrollgruppen in Bezug auf relevante Eigenschaften bestimmt. Die Empfehlung von Ho et al. zur Auswahl des am besten geeigneten Matchingverfahrens lautet, verschiedene Modelle und Verfahren durchzuführen und das Verfahren zu wählen, welches die Balance, also die Ähnlichkeit, der Gruppen maximiert. Im Gegensatz zur Evaluation der Endpunkte gibt es kein Problem des multiplen Testens beim Durchführen mehrerer konkurrierender Matchingverfahren [29]. Das Einbeziehen von exaktem Matching verbesserte die Ähnlichkeit der Gruppen gegenüber ausschließlichem Propensity-Score Matching. Auch wenn die Grundgesamtheit der Personen, aus denen eine Kontrollgruppe gebildet werden konnte, mit 205 738 Versicherten sehr umfangreich ist, wird mit zunehmender Anzahl der Variablen im exakten Matching die resultierende gematchte Gruppe kleiner. Rosenbaum und Rubin bezeichnen den resultierenden Effekt als „bias due to incomplete matching“ [30]. Beim Propensity-Score Matching stehen verschiedene Algorithmen zur Bildung der Kontrollgruppe zur Wahl. Die bekanntesten sind das Nearest-neighbor Verfahren und Optimal Matching. Beim Vergleich der Verfahren zeigte sich, dass beide Verfahren zu sehr ähnlichen Gruppenzusammensetzung führen. Diese Beobachtung wird durch eine umfangreiche Simulationsstudie von Austin unterstützt, welche ebenfalls die Ähnlichkeit der Ergebnisse der Verfahren (bei hinreichender Größe der Grundgesamtheit) feststellt [31]. Aufgrund der höheren Geschwindigkeit des Algorithmus fiel hier die Wahl auf das Nearest-neighbor Verfahren.

Überleben und Krankenhausaufnahmen

In der Intention-to-treat Analyse war die Chance für Versicherte mit telemedizinischer Intervention, nach einem Jahr noch am Leben zu sein, im Vergleich zur Kontrollgruppe deutlich erhöht (adjustiertes OR: 1,47, 95%-CI: 1,21 - 1,80, p < 0,001). Nach zwei Jahren war der Effekt ähnlich groß (adjustiertes OR: 1,51, 95%-CI: 1,28 - 1,77, p < 0,001). Dies bestätigt die Robustheit der Ergebnisse in den ersten zwei Jahren. In einer nach Geschlecht stratifizierten Analyse wurde gezeigt, dass Frauen hinsichtlich des Überlebens stärker von der Telemedizin profitierten als Männer. Um die Langzeiteffekte zu beurteilen, wurde eine Survival-Analyse durchgeführt. Diese bestätigte die Beobachtungen für die ersten beiden Jahre, danach glichen sich die Überlebensraten an. Die endgültige Beurteilung der Langzeiteffekte könnte aber nur auf Basis zusätzlicher Daten erfolgen.

Ein Cochrane-Review bestärkt den Nutzen von strukturierter telefonischer Unterstützung von Menschen mit Herzinsuffizienz hinsichtlich der Gesamtmortalität (22 Studien, RR: 0,87; 95%-CI: 0,77 - 0,98) und der Anzahl der Herzinsuffizienz-bedingten Krankenhausaufenthalte (16 Studien, RR: 0,85; 95%-CI: 0,77 - 0,93). Nicht-invasives Telemonitoring reduzierte ebenfalls die Gesamtmortalität (17 Studien, RR: 0,80; 95%-CI: 0,68 - 0,94) und die Anzahl der Herzinsuffizienz-bedingten Krankenaufenthalte (8 Studien, RR: 0,71; 95%-CI: 0,60 - 0,83) [12]. Aufgrund der räumlichen (aber nicht methodischen) Nähe ist die Studie von Köhler et al. zu erwähnen. In der randomisierten Studie TIM-HF mit insgesamt 710 Menschen mit Herzinsuffizienz in den NYHA-Stadien II und III kann kein signifikanter Effekt der Intervention auf die Mortalität nachgewiesen werden [32].

Ausblick: Subgruppenanalyse des Überlebens

Nachdem in der Gesamtgruppe ein positiver Effekt der Intervention auf das Überleben festgestellt wurde, könnte eine weiterführende Analyse des Datensatzes ermitteln, ob es Unterschiede zwischen Subgruppen gibt. Eine Meta-Analyse von Nakamura et al. über Telemedizin-basierte Versorgungsprogramme für Menschen mit Herzinsuffizienz liefert Hinweise, dass Unterschiede in Subgruppen bestehen. In die Meta-Analyse wurden 13 Studien mit einer Gesamtzahl von 3 337 Personen eingeschlossen. Der Einsatz Telemedizin-basierter Versorgungsprogramme für Menschen mit Herzinsuffizienz resultierte in einer signifikant niedri-

geren Sterberate ($RR = 0,76$, 95%-CI = $0,62 – 0,93$) im Vergleich zur Kontrollgruppe. In Bezug auf das Sterberisiko gab es Hinweise auf Unterschiede zwischen Subgruppen:

- Die Versorgungsprogramme waren effektiver bei Gruppen mit einem geringeren Durchschnittsalter als bei denjenigen mit einem hohen Durchschnittsalter ($RR = 0,71$ gegenüber der Kontrollgruppe vs. $RR = 0,79$, $p = 0,60$).
- Die Versorgungsprogramme waren effektiver bei Menschen mit einer hohen Krankheitsschwere als bei denjenigen mit einer geringeren Krankheitsschwere ($RR = 0,63$ vs. $RR = 0,86$, $p = 0,13$).
- Die Versorgungsprogramme waren effektiver bei häufiger Untersuchung der Patientinnen und Patienten als bei seltener Untersuchung ($RR = 0,62$ vs. $RR = 0,89$, $p = 0,07$).
- Die Versorgungsprogramme waren in Kombination mit einem Medikamentenmanagement effektiver als ohne Medikamentenmanagement ($RR = 0,65$ vs. $RR = 0,85$, $p = 0,19$) [33].

Die von Nakamura et al. betrachteten Parameter Alter und Krankheitsschwere liegen auch im Datensatz vor. Weitere Subgruppenanalysen hinsichtlich Medikation, Vorliegen von Komorbiditäten und Wohnregion könnten in Erwägung gezogen werden.

Gesundheitskosten

In der durchgeföhrten Analyse der durchschnittlichen Gesundheitskosten im Zeitraum nach Interventionsbeginn zeigten sich schwach positive Effekte der Intervention. Es ist zu vermuten, dass bei den Gesundheitskosten insbesondere Ko- und Multimorbidität einen großen Einfluss haben. Eine Möglichkeit eine valide Langzeitanalyse der Gesundheitskosten durchzuführen, wäre die Anwendung von Linear Mixed Models [34], aber auch hier wäre zunächst eine Verbesserung im Längsschnitt der Datengrundlage wünschenswert.

Im Cochrane-Review berichteten drei (von neun) Studien über strukturierte telefonische Unterstützung und eine (von sechs) Telemonitoring-Studien über einen Rückgang der Gesundheitskosten. Zwei Telemonitoring-Studien zeigten einen Anstieg der Kosten, sowohl aufgrund der Interventionskosten als auch aufgrund eines erhöhten medizinischen Ma-

nagementaufwands [12]. In einer italienischen Telemonitoring-Studie wurden 48 ältere Patientinnen und Patienten mit einem hohen CHF-Risiko für 20 Monate nachbeobachtet. Vier Personen (8,3%) brachen die Beratung ab, 13 Personen (29,5%) starben aufgrund kardialer Ursachen. Die Krankenhauseinweisungen wegen Herzinsuffizienz gingen im Jahr nach der Einschreibung im Vergleich zum Vorjahr zurück und die Gesundheitsausgaben reduzierten sich von 116 856 Euro/Jahr auf 40 065 Euro/Jahr [35].

Ausblick: Multimorbidität

Aktuelle Studien zu Programmen zur telefonischen Unterstützung bzw. Telemonitoring bei Herzinsuffizienz untersuchen häufig Anwendungen für mehrere chronische Erkrankungen gleichzeitig. Chronisch obstruktive Lungenerkrankungen (COPD) und CHF bestehen (insb. bei älteren Menschen) häufig nebeneinander, was die Lebensqualität der Betroffenen beeinträchtigt und die Mortalität erhöht. Bernocchi et al. führten eine randomisierte kontrollierte Studie mit Patientinnen und Patienten durch, die an CHF und COPD litten. Die Autoren untersuchten die Durchführbarkeit sowie die Effektivität eines Telemedizin-basierten Rehabilitationsprogrammes über einen Zeitraum von 4 Monaten. Eine weitere Testung erfolgte 2 Monate nach Beendigung des Rehabilitationsprogrammes. Insgesamt wurden 112 Personen auf die Interventions- und auf die Kontrollgruppe randomisiert. Die Interventionsgruppe erhielt ein Trainingsprogramm durch einen Physiotherapeuten, wurde wöchentlich von einer Krankenpflegerin kontaktiert und erhielt ein Pulsoximeter sowie ein portables EKG-Gerät. In der Interventionsgruppe betrug die Zeitspanne bis zur Hospitalisierung oder Tod (kombinierter Endpunkt) im Durchschnitt 113,4 Tage im Gegensatz zu 104,7 Tage in der Kontrollgruppe ($p = 0,048$) [36].

Oksman et al. untersuchten in ihrer Studie über einen Zeitraum von 12 Monaten die Kosten-effektivität eines Telemedizin-basierten Versorgungsprogrammes für Menschen mit mindestens einer Erkrankung aus den Bereichen Typ-2-Diabetes (T2D), koronare Herzkrankheit (CAD) oder Herzinsuffizienz (Priorisierung bei mehr als einer Erkrankung: CHF, CAD, T2D). Es wurden 1 570 Patientinnen und Patienten randomisiert auf die Interventions- bzw. Kontrollgruppe verteilt. Die Interventionsgruppe wurde regelmäßig telefonisch durch speziell für diese Zwecke ausgebildete Krankenpflegerinnen und -pfleger kontaktiert und beraten. Während die Intervention in der Kosten-Nutzen-Analyse einen positiven Effekt auf die Lebens-

qualität von Menschen mit Diabetes (Kosten-Nutzen-Verhältnis (ICER) = 20 000 Euro pro Quality-Adjusted Life Year) oder koronarer Herzkrankheit (ICER = 40 278 Euro pro QALY) hatte, stiegen die Gesundheitskosten bei CHF-Patienten bei unveränderter Lebensqualität an [37].

In einer randomisierten klinischen Studie zur telefonischen Unterstützung für 171 Menschen mit CHF, COPD oder T2D (drei verschiedene Interventionen in drei Studienzentren) wurde ermittelt, dass Angst und Depressionen mit der Intervention deutlich abnahmen. Krankenhausinweisungen, Krankenhaustage, Notfallbesuche, ambulante Besuche und Kosten unterschieden sich nicht signifikant zwischen den Gruppen [38].

4.1 Stärken und Schwächen der Studien

Eine Stärke dieser Analyse ist, dass die Intervention in der Versorgungsrealität durchgeführt wurde. Es wird eine breite Auswahl von Versicherten beider Geschlechter und in allen Altersgruppen und mit unterschiedlichen NYHA-Stadien angesprochen. Die analysierten Patientinnen und Patienten repräsentieren eine wenig selektierte, breite Gruppe einschließlich älterer und schwer erkrankter Menschen mit NYHA-Stadium IV. Die erzielten Ergebnisse sind über die Zeit konsistent, eine Überprüfung der Langzeiteffekte darüber hinaus wäre allerdings wünschenswert.

Die Grundlage der Untersuchung bilden die Versichertendaten der AOK Nordost. Diese dienen in erster Linie zu Abrechnungszwecken und bilden das tatsächliche Versorgungsgeschehen nicht immer vollständig und realistisch ab. So wurden beispielsweise für die Evaluation wichtige Parameter wie das NYHA-Stadium nicht einheitlich und in vielen Fällen auch nicht zum Zeitpunkt des Einschlusses in das *Cordiva*-Programm erfasst, wodurch eine Interpretation der Entwicklung des NYHA-Stadiums erschwert wird. Eine weitere Schwäche der Untersuchung ist, dass nur eine Angabe zur Wohnregion der Patienten (aktuelle oder zuletzt bekannte Postleitzahl) für die gesamte Evaluationsdauer vorliegt. Die Wohnregion zum Zeitpunkt der Evaluation beruht somit auf der Annahme, dass Versicherte während des Interventionszeitraumes nicht zwischen den Regionen umgezogen sind.

4.2 Schlussfolgerung

Die Evaluation des Programms *Cordiva* auf der Basis von Routinedaten der AOK Nordost zeigt, dass die Intervention, bestehend aus telefonischer Beratung und telemedizinischen Waagen, positive Effekte auf die Überlebenswahrscheinlichkeit nach einem und zwei Jahren hat. Gleichzeitig verringern sich die Gesundheitskosten, wobei dieser Effekt bei Versicherten aus Berlin gering war. Eine signifikante Reduktion der Kosten wird jedoch in den Regionen außerhalb Berlins beobachtet. In Übereinstimmung mit der Literatur sprechen die Ergebnisse für eine Ausweitung niederschwelliger telemedizinischer Anwendungen für Menschen mit chronischer Herzinsuffizienz.

5 Zusammenfassung

Im Rahmen der vorliegenden Analyse wird das Interventionsprogramm *Cordiva* der AOK Nordost für Menschen mit Herzinsuffizienz auf der Basis von Abrechnungsdaten evaluiert. Die Intention-to-treat Analyse zeigt positive Effekte der telemedizinischen Intervention für die teilnehmenden Versicherten. Das adjustierte OR für Überleben nach einem Jahr beträgt 1,47 gegenüber der gemachten Kontrollgruppe (95%-CI: 1,21 - 1,80, $p < 0,001$) und ist auch nach zwei Jahren ähnlich groß (adjustiertes OR = 1,51, 95%-CI: 1,28 - 1,77, $p < 0,001$). Bei den Gesundheitskosten unterscheiden sich die Ergebnisse in städtischen (-18 Euro pro Quartal und Versicherten) und ländlichen Regionen (-276 Euro pro Quartal und Versicherten). Die Ergebnisse deuten darauf hin, dass die Intervention insgesamt wirksam und für große Patientengruppen auch gesundheitsökonomisch effizient ist.

The analysis evaluates the intervention program *Cordiva* (AOK Nordost) for patients with heart failure on the basis of reimbursement data. The intention-to-treat analysis yields positive effects of the telemedical intervention for the participants. The adjusted OR for survival after one year is 1.47 compared to the control group (CI 95%: 1.21 - 1.80, $p < 0.001$) and is similarly large after two years (adjusted OR = 1.51, 95% CI: 1.28 - 1.77, $p < 0.001$). For health care costs, the results differ in urban (-18 euros per quarter year and insured person) and rural regions (-276 euros per quarter year and insured person). The results indicate that the intervention is overall effective and also health-economically efficient for large patient groups.

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Anhang - Wissenschaftliche Artikel

Herold R, van den Berg N, Dörr M, Hoffmann W. Telemedical Care and Monitoring for Patients with Chronic Heart Failure has a positive Effect on Survival. *HEALTH SERVICES RESEARCH*. 2018; 53(1):532-555.

Herold R, Hoffmann W, van den Berg N. Telemedical Monitoring of Patients with Chronic Heart Failure has a positive Effect on Total Health Costs. *BMC HEALTH SERVICES RESEARCH*. 2018; 18:271.

Telemedical Care and Monitoring for Patients with Chronic Heart Failure Has a Positive Effect on Survival

*Robert Herold, Neeltje van den Berg, Marcus Dörr,
and Wolfgang Hoffmann*

Background. Telemedical care and monitoring programs for patients with chronic heart failure have shown beneficial effects on survival in several small studies. The utility in routine care remains unclear.

Methods. We evaluated a large-sized telemedicine program in a routine care setting, enrolling in total 2,622 patients (54.7 percent male, mean age: 73.7 years) with chronic heart failure. We used reimbursement data from a large statutory health insurance and approached a matched control analysis. In a complex propensity score matching procedure, 3,719 suitable controls (54.2 percent male, mean age: 74.5 years) were matched to 1,943 intervention patients (54.1 percent male, mean age: 74.4 years). The primary endpoint of our analysis was survival after 1 year.

Results. Analyses revealed a higher survival probability among subjects of the intervention group compared to controls group after 1 year (adjusted OR: 1.47, CI 95 percent: 1.21–1.80, $p < .001$) and 2 years (adjusted OR: 1.51, CI 95 percent: 1.28–1.77, $p < .001$), respectively.

Conclusions. The probabilities to survive after 1 and 2 years were significantly increased in the intervention group. Our findings confirm previous results of controlled trials and importantly indicate that patients with chronic heart failure may benefit from telemonitoring programs in routine care.

Key Words. Chronic heart failure, telemedical care, telemedical monitoring, reimbursement data, routine data, propensity score matching

Chronic heart failure (CHF) is a main cause of morbidity, hospital admission, and death in Germany (Statistisches Bundesamt 2014, 2015). Both the prevalence and incidence rate of CHF are continuously increasing because of the strong positive correlation with increasing age (Bleumink et al. 2004) and improved treatment options for patients with acute myocardial infarction, heart valves diseases, and cardiomyopathies resulting in elevated survival rates (Roger 2013).

However, the prognosis of CHF is still poor. Thus, a large-scale European population-based prospective cohort study in the elderly population concludes that heart failure continues to be a fatal disease, with only 35 percent surviving patients 5 years after the first diagnosis (Bleumink et al. 2004).

Telemedicine programs were developed to improve monitoring and therapy adherence of patients with chronic diseases (Inglis et al. 2010). Telemonitoring of patients with CHF can potentially facilitate early detection warning signs of impending decompensation and thereby prevent hospitalization. A recent review of van den Berg et al. shows that telemedical measures can be implemented also in an older population. In particular, intervention measures that are based on personal contact with the patient seem to be successful (van den Berg et al. 2012). Chaudhry et al. (2007) review telemonitoring programs especially for patients with CHF and conclude that telemonitoring may be an effective strategy for disease management in high-risk heart failure patients with respect to reduction in hospitalizations (all-cause and heart failure-related hospitalizations) and mortality.

In this study, we evaluate the telemonitoring program “AOK-Curaplan Herz Plus” for patients with CHF, comprising the provision of information leaflets about heart failure, a modem-connected scale, and telephone coaching by special trained nurses (Gesellschaft für Patientenhilfe DGP mbH 2009). Primary outcome of this investigation is survival 1 year after enrollment into the intervention program. The secondary outcomes are survival after 2 years and hospitalization. Further, an analysis of survival after 1 year is conducted in the patient group with a documented beginning of the intervention (treated group).

METHODS

Intervention Program

AOK-Curaplan Herz Plus is a telemedicine program for CHF patients, offered by the statutory health insurance AOK Nordost in Germany. The

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AOK Nordost is a statutory health insurance with insured persons living in the German federal states of Berlin, Brandenburg, and Mecklenburg-Western Pomerania in northeastern Germany.

The program consists of regular telephone coaching and counseling, information leaflets about disease-related themes, and a digital scale for weight control. Telephone coaching and counseling is conducted by trained nurses in a telemedicine service center, specialized on medical services. Telephone contacts are conducted every 4 to 12 weeks, dependent on the patients' individual needs. If needed, patients can contact the telemedicine service center any time. In case of a deteriorating health situation, the nurses give concrete recommendations or contact the treating physician. AOK-Curaplan Herz Plus started in 2006 and is still running in the German federal states of Berlin and Brandenburg.

Participants

The intervention was implemented in a regular care setting. Patients with a diagnosis of CHF (ICD-10 diagnosis codes I50.12, I50.13, or I50.14 and NYHA class > I) with a high risk for a heart failure-related hospitalization were included. High risk was defined as a prior hospitalization due to heart failure. Exclusion criterion was the presence of any diagnosed mental disorder (ICD-10 F00-F99) at the time of recruitment. The recruitment of patients was divided into two phases: From 2006 to 2009, eligible patients, insured with the statutory health insurance, were included by general practitioners and cardiologists in private practices. Since 2009, possible participants were retrieved from the database from the statutory health insurance AOK Nordost. All patients, included in the telemedicine program, provided written informed consent.

Study Design

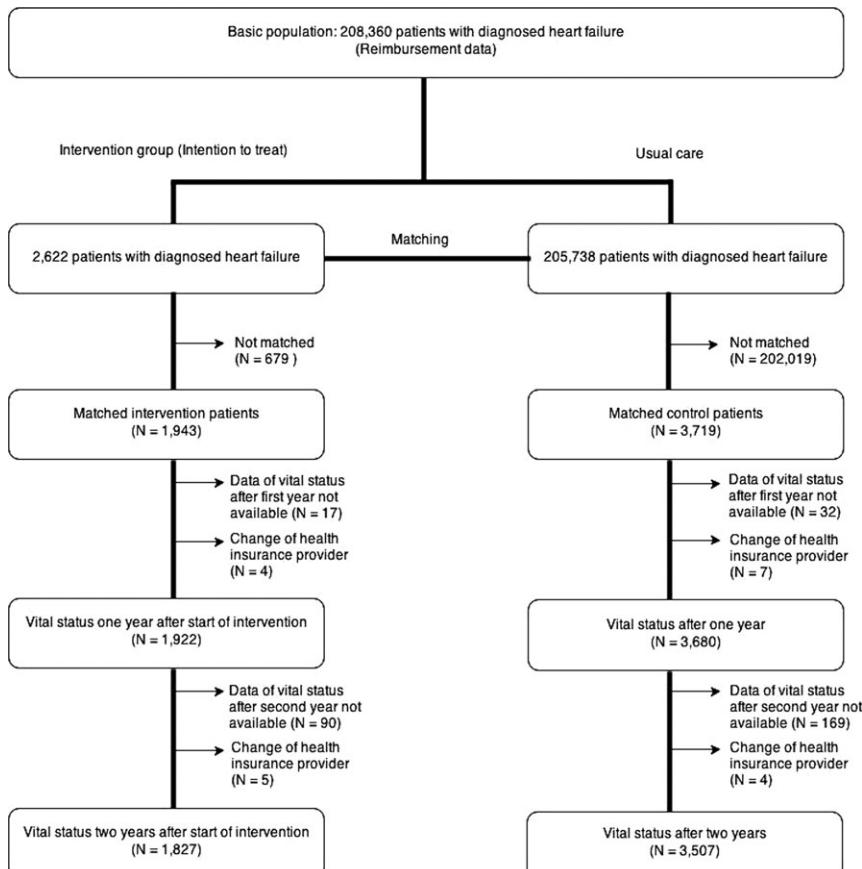
To analyze the effect of the intervention on the survival of all participating patients (intention-to-treat) compared to an appropriate control group, we implemented a matched control analysis (Stuart and Rubin 2007). The control group was compiled using a combination of propensity score and exact matching (see section “matching” for further details). The control patients were retrieved from the database of the statutory health insurance. For patients of the intervention group, the quarter year of enrollment served as baseline. The baseline for patients of the control group was set as the quarter year of matching.

Multivariate regression models were performed to analyze the effects of the intervention (Ho et al. 2007). Figure 1 shows the study flow from baseline to the analysis.

Variable Definitions

Matching procedure and statistical analyses were based on routine data (reimbursement data) only. Most baseline variables refer to the quarter year of enrollment, because reimbursement is carried out on the basis of quarter

Figure 1: Consort Diagram Showing the Selection of Patients to Be Included in the Analysis (Intention-to-Treat Analysis)



years. Exceptions are hospital admissions (all causes and related to CHF) and emergency hospitalizations, which refer to the quarter of enrollment and three prior quarter years (hereafter denoted as “baseline year”). Total health costs refer to a quarter mean of total health costs during the baseline year. We defined baseline NYHA class as the measure of NYHA stage which was identified temporally closest prior to the quarter of enrollment. In the German health care system, NYHA is collected in the administrative database and reimbursement data as part of every CHF diagnosis, usually in case of CHF-specific diagnostic or therapeutic activities. The most recent diagnosed NYHA class was in average 1.50 quarter years before enrollment in the intervention group (range 0–18, median 1.0) and 1.51 quarter years in the control group (range 0–18, median 1.0).

For patients’ residential area, level of care, and retirement home status, information was only available for the time of data acquisition (July 2012). Survival was measured as the absence of death. Insured persons who changed the health insurance provider within the first year after enrollment were excluded from the analysis.

Matching Procedure

The control group was retrieved from the database of the statutory health insurance. The initial sample consisted of all patients with a diagnosis of CHF registered in the database. We combined exact and propensity score matching using a nearest neighbor method (greedy algorithm) with restrictions in chosen covariates (matching without replace, two controls per case at the maximum) (Rubin 1973; Ho et al. 2007).

Intervention patients were matched at their quarter year of enrollment (respectively the quarter of starting the intervention in the sensitivity analysis), and controls were drawn dynamically. Dynamically means that controls could be matched to intervention patients every quarter year as long as they were insured, still alive, and not matched in a prior quarter year.

The following variables were considered for the exact matching procedure: sex, 5-year-age group, NYHA class, the number of hospital admissions in the 12 months prior to inclusion, cost category (23 categories of various ranges, representing the medical costs of the patients/quarter year), and the presence of any mental or behavioral disorders (ICD-10: F00–F99). In addition, medication in six groups of active agents used for treatment of CHF (angiotensin-converting enzymes, beta-blockers, renin inhibitors, glycosides, diuretics, and AT1 receptor blockers) and mental and behavioral disorders in

11 diagnoses groups (organic, including symptomatic, mental disorders [F00–F09], mental and behavioral disorders due to psychoactive substance use [F10–F19], schizophrenia, schizotypal, and delusional disorders [F20–F29], mood [affective] disorders [F30–F39], neurotic, stress-related, and somatoform disorders [F40–F49], behavioral syndromes associated with physiological disturbances and physical factors [F50–F59], disorders of adult personality and behavior [F60–F69], mental retardation [F70–F79], disorders of psychological development [F80–F89], behavioral and emotional disorders with onset usually occurring in childhood and adolescence [F90–F98], and unspecified mental disorders [F99–F99]) were included as further propensity score matching criteria. The reason for including mental disorders in the matching procedure was that, although the existence of any mental disorder was an exclusion criterion, a high number of patients with these diagnoses were included in the intervention program.

All matched patients received a statistical weight (1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified). The statistical weighting was described by the authors of the used matching software (Ho et al. 2011).

Statistical Analysis

The main analysis was performed according to an intention-to-treat approach, including all matched patients. In the descriptive baseline analysis, group differences between the matched intervention and the matched control group in continuous variables were compared using unpaired two-sample *t*-tests, while chi-square tests were used to compare categorical variables.

Analysis of the primary endpoint (survival after 1 year) was conducted by logistic regression models. All models were adjusted by age, sex, NYHA class, CHF-related hospitalization, medication, mental disorders, and the dichotomized residential area (urban = Berlin vs. rural = Brandenburg, Mecklenburg-Western Pomerania, and other). Age was modeled as a continuous variable. As a secondary endpoint, we examined the number of hospitalizations per patient. We determined the mean numbers of total hospital admissions and CHF-related hospital admission per year 1 and 2 years after baseline, respectively. We only considered years where the patient was (at least 1 day) alive. Group differences in negative binomial regression models were expressed by incidence risk ratios (IRRs).

We considered a p -value <0.05 to show statistically significant differences in all comparisons. Statistics were calculated using *R* statistical software, version 3.0 (R Foundation for Statistical Computing, Vienna, Austria). We used the *R* packages “MatchIt” (Ho et al. 2011) for data matching, “Survey” (Lumley 2004) for weighted descriptive analyses, and “base” (R Core Team 2015) for fitting the regression models.

To examine the impact of the dropouts on the results of the intervention, a sensitivity analysis under the assumption that all patients missing from follow-up died was performed.

Furthermore, the intervention program was run by a third-party supplier. Detailed information on the individual patients’ treatment was not known. Hence, another sensitivity analysis was performed with the subgroup of 1,835 patients with a documented start of the intervention program (treated group). Because of a high variation in time between enrollment and start of the intervention program among the patients, a separate matching was performed. The quarter year of the start of the intervention served as baseline. In the treated analysis, the odds ratios were fitted in the same regression models as the intention-to-treat models.

RESULTS

Intention-to-Treat Analysis

Overall, 1,943 intervention patients (74.1 percent of the entire intervention group) could be matched to 3,719 control patients. Information on the vital status for the 12-month follow-up was available for 1,922 patients in the intervention group (98.9 percent of matched intervention group) and 3,680 patients in the control group (99.0 percent). At the 2-year follow-up, the vital status was known for 1,827 patients in the intervention (94.0 percent) and 3,507 patients in the control group (94.3 percent), respectively.

Baseline Characteristics

Table 1 shows the distribution of parameters at baseline, defined as the quarter year of enrolment in the intervention program for patients of the intervention group, and the quarter year of matching for patients of the control group.

The overall and the matched intervention group showed only slight differences in most variables. Comparing the matched and the unmatched intervention group, statistically significant differences can be seen in the variables

Table 1: Baseline Characteristics of the Intervention Patients and Controls

Variable	Mean (SD)/N (%)*			<i>p</i> -value (Intervention Groups)	<i>p</i> -value (Matched Groups)
	Overall Intervention Group (N = 2,622)	Unmatched Intervention Group (N = 679)	Matched Intervention Group (N = 1,943)		
Sex					
Male	1,439 (54.88) 1,183 (45.12)	387 (57.00) 292 (43.00)	1,052 (54.14) 891 (45.86)	2,014 (54.15) 1,705 (45.85)	.2146
Age groups					
≤40 years	7 (0.27)	7 (1.03)	—	—	<.0001
41–45 years	18 (0.69)	10 (1.47)	8 (0.41)	15 (0.41)	—
46–50 years	42 (1.60)	20 (2.95)	22 (1.13)	42 (1.12)	—
51–55 years	72 (2.75)	26 (3.83)	46 (2.37)	88 (2.36)	—
56–60 years	110 (4.20)	41 (6.04)	69 (3.55)	132 (3.54)	—
61–65 years	176 (6.71)	49 (7.22)	127 (6.54)	243 (6.52)	—
66–70 years	414 (15.79)	109 (16.05)	305 (15.70)	585 (15.72)	—
71–75 years	561 (21.40)	135 (19.88)	426 (21.92)	816 (21.93)	—
76–80 years	595 (22.69)	154 (22.68)	441 (22.70)	845 (22.73)	—
81–85 years	390 (14.87)	76 (11.19)	314 (16.16)	601 (16.16)	—
86–90 years	200 (7.63)	41 (6.04)	159 (8.18)	304 (8.18)	—
91–95 years	37 (1.41)	11 (1.62)	26 (1.34)	49 (1.33)	—
Age [years]	73.73 (SD 9.64)	71.70 (SD 11.09)	74.44 (SD 8.97)	74.48 (SD 9.04)	<.0001
NYHA class					
NYHA I	32 (1.45)	13 (4.91)	19 (0.98)	36 (0.98)	—
NYHA II	675 (30.57)	61 (23.02)	614 (31.60)	1,175 (31.60)	—
NYHA III	877 (39.72)	98 (36.98)	779 (40.09)	1,491 (40.09)	—
NYHA IV	624 (28.26)	93 (35.09)	531 (27.33)	1,016 (27.33)	—
Missing	414	414	—	—	—

continued

Table 1: *Continued*

Variable	Mean (SD)/N (%)*			<i>p-value</i> (Matched Groups)
	Overall Intervention Group (N = 2,622)	Unmatched Intervention Group (N = 679)	Matched Intervention Group (N = 1,943)	
Hospital admissions (baseline year)				
All causes	2.55 (SD 2.14)	2.57 (SD 3.04)	2.54 (SD 1.73)	.2.53 (SD 1.88)
Related to CHF	1.38 (SD 1.28)	1.39 (SD 2.05)	1.37 (SD 0.86)	1.37 (SD 0.86)
Emergency hospitalizations (baseline year)				
All causes	0.64 (SD 1.27)	0.60 (SD 1.24)	0.65 (SD 1.27)	0.55 (SD 1.30)
Total health costs [Euros] (quarterly mean in baseline year)	3,918.40 (SD 3,904.32)	4,421.21 (SD 5,754.73)	3,746.80 (SD 3,007.20)	3,750.10 (SD 3,021.40)
All regions	3,748.43 (SD 3,670.68)	3,815.41 (SD 5,175.95)	3,722.90 (SD 2,899.90)	3,958.60 (SD 3,502.80)
Urban	4,501.74 (SD 4,572.86)	7,604.49 (SD 7,399.72)	3,819.40 (SD 3,313.30)	3,676.60 (SD 2,829.30)
Rural				<.0001
Health costs [Euros] (quarterly mean in baseline year)				.3777
Inpatient	2,604.70 (SD 3,162.36)	3,016.13 (SD 4,750.57)	2,464.30 (SD 2,375.60)	2,403.00 (SD 2,322.30)
Outpatient	317.22 (SD 744.13)	379.22 (SD 996.14)	296.06 (SD 634.63)	293.53 (SD 763.82)
Drugs	562.47 (SD 910.85)	608.59 (SD 1,200.42)	546.74 (SD 787.84)	563.50 (SD 751.29)
Remedy	44.76 (SD 121.90)	31.57 (SD 87.54)	49.26 (SD 131.30)	39.43 (SD 125.86)
Adjuvant	98.47 (SD 224.12)	103.78 (SD 254.59)	96.66 (SD 212.76)	109.62 (SD 225.80)
Home health care	117.91 (SD 490.44)	91.40 (SD 368.55)	126.95 (SD 525.38)	140.06 (SD 425.66)
Travel costs	166.01 (SD 305.45)	183.34 (SD 389.37)	160.09 (SD 270.80)	198.21 (SD 304.08)
Rehabilitation	6.87 (SD 44.45)	7.18 (SD 46.32)	6.76 (SD 43.81)	2.71 (SD 26.82)
Medication (percentage "yes" per active agent in baseline quarter year)				
Angiotensin-converting enzymes	1,119 (42.94)	274 (41.33)	845 (43.49)	1,637 (44.01)
Beta-blockers	1,643 (63.05)	382 (57.62)	1,261 (64.90)	2,340 (62.93)
				.0009
				.1515

continued

Table 1: *Continued*

Variable	Mean (SD)/N (%)*					
	Overall Intervention Group (N = 2,622)	Unmatched Intervention Group (N = 679)	Matched Intervention Group (N = 1,943)	Matched Control Group (N = 3,719)	p-value (Intervention Groups)	p-value (Matched Groups)
Renin inhibitors	45 (1.73)	9 (1.36)	36 (1.85)	51 (1.36)	.501	.1853
Cardiac glycosides	372 (14.27)	93 (14.03)	279 (14.36)	548 (14.73)	.8833	.7388
Diuretics	1,643 (63.05)	345 (52.04)	1,298 (66.80)	2,507 (67.40)	<.0001	.6727
AT1 receptor blocker	532 (20.41)	147 (22.17)	385 (19.81)	651 (17.51)	.2133	.0360
Mental and behavioral disorders (baseline quarter year)						
Yes	983 (37.72)	240 (36.1)	743 (38.24)	1,421 (38.20)	.3736	—
No	1,623 (62.28)	423 (63.8)	1,200 (61.76)	2,298 (61.80)		
Missing	16	16	—	—		
Residential area						
Berlin	2,032 (77.50)	571 (84.09)	1,461 (75.19)	969 (26.06)	<.0001	<.0001
Brandenburg	524 (19.98)	88 (12.96)	436 (22.44)	1,482 (39.84)		
Mecklenburg-Western Pomerania	40 (1.53)	13 (1.91)	27 (1.39)	1,235 (33.20)		
Other	26 (0.99)	7 (1.03)	19 (0.98)	34 (0.90)		
Comorbidities, stationary diagnoses						
Diabetes (E10–E14)	1,198 (45.69)	248 (36.52)	950 (48.89)	1,944 (52.27)	<.0001	.0172
Cancer (C00–C97)	315 (12.01)	67 (9.87)	248 (12.76)	481 (12.95)	.0536	.8788
Kidney disease (N17–N19)	1,153 (43.97)	223 (32.84)	930 (47.86)	1,862 (50.08)	<.0001	.1204
COPD (J44)	635 (24.22)	118 (17.38)	517 (26.61)	1,002 (26.94)	<.0001	.8144

*Matched patients received a statistical weight: 1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified.

age, NYHA class, total health costs, three cost sections (inpatient, outpatient, and remedy), medication (beta-blockers and diuretics), residential area, and level of care.

Around 54 percent of the patients in both matched groups were male. The mean of age was approximately 74 years in both groups (intervention group: 74.44 years, SD 8.97, control group: 74.48 years, SD 9.04). NYHA II and III were the most frequent NYHA classes. The mean number of hospital admissions (all causes) was 2.54 per year (SD 1.73) during the baseline quarter year and three previous quarter years for the intervention group (control group: 2.53, SD 1.88), while 1.37 (SD 0.86) hospital admissions were related to CHF in both groups. The total health costs per quarter year in the baseline year averaged 3,746.80 euros (SD: 3,007.20) in the intervention group and 3,750.10 euros (SD: 3,021.40) in the control group. In the intervention group, 743 patients (38.24 percent) had at least one diagnosed mental disorder (ICD-10 Chapter V) in the baseline quarter year.

With respect to comorbidities, the prevalence of cancer, kidney disease, and COPD was similar between the matched intervention and control group. Only the prevalence for diabetes differs (48.89 percent in the intervention group vs. 52.27 percent in the control group; $p = .017$).

The intervention and control group differed significantly with respect to the frequencies of AT1 receptor blocker medication, the number of emergency hospitalizations, the residential area, the level of care, and the rate of patients living in retirement houses.

Survival

Table 2 shows the weighted number of patients who were alive at the 1-year follow-up. Of 1,922 patients of the intervention group, 1,711 (89.02 percent) were still alive compared to 3,179 of 3,680 (86.37 percent) in the control group. The survival rates among the sexes were similar in the control group (male: 86.44 percent, female: 86.30 percent), whereas 90.27 percent of all females in the intervention but only 87.96 percent of all males survived the first year.

At the 2-year follow-up, the probability to survive was increased by 5.7 percentage points in the intervention group compared to the control group (79.4 percent vs. 73.7 percent). In the intervention group, the rate of surviving patients converged among the sexes (male: 79.03 percent, female: 79.76 percent). Again, in the control group, the likelihood to survive did not differ among the sexes (Table 2).

Table 2: Survival and Hospitalization after 1 and 2 years

Survival		N (%)*	Logistic Regression Models (matched patients only)			
			Total Intervention Group	Matched Intervention Group	Matched Control Group	OR of Study Group (adjusted, reference: control group)
1-year follow-up						
Group size			2,574	1,922	3,680	
All patients	Alive	2,261 (87.84)	1,711 (89.02)	3,179 (86.37)	1.47 (CI 95%: 1.21–1.80)	.0002
	Dead	313 (12.16)	211 (10.98)	501 (13.63)		
Male	Alive	1,213 (86.33)	913 (87.96)	1,719 (86.44)	1.26 (CI 95%: 0.97–1.65)	.0906
	Dead	192 (13.67)	125 (12.04)	270 (13.56)		
Female	Alive	1,048 (89.65)	798 (90.27)	1,460 (86.30)	1.75 (CI 95%: 1.29–2.38)	.0003
	Dead	121 (10.35)	86 (9.73)	232 (13.70)		
2-year follow-up						
Group size			2,450	1,837	3,507	
All patients	Alive	1,935 (78.98)	1,450 (79.37)	2,584 (73.67)	1.51 (CI 95%: 1.28–1.77)	<.0001
	Dead	515 (21.02)	377 (20.63)	924 (26.33)		
Male	Alive	1,044 (77.91)	780 (79.03)	1,399 (73.89)	1.43 (CI 95%: 1.15–1.79)	.0016
	Dead	296 (22.09)	207 (20.97)	494 (26.11)		
Female	Alive	891 (80.27)	670 (79.76)	1,185 (73.41)	1.59 (CI 95%: 1.25–2.02)	.0002
	Dead	219 (19.73)	170 (20.24)	429 (26.59)		

continued

Table 2: *Continued*

Hospitalizations per Patient and Year		Mean (SD)				Negative Binomial Regression Models (Matched Patients Only)	
		Total Intervention Group	Matched Intervention Group	Matched Control Group	IRR of Study Group: (Adjusted Reference: Control Group)		
1-year follow-up							
All patients	All causes	1.55 (SD 2.00)	1.56 (SD 1.93)	1.57 (SD 2.03)	1.01 (CI 95%: 0.93–1.09)	.8939	
	Related to CHF [†]	0.60 (SD 1.15)	0.61 (SD 1.10)	0.61 (SD 1.13)	1.10 (CI 95%: 0.98–1.23)	.0932	
2-year follow-up							
All patients	All causes	1.33 (SD 1.86)	1.53 (SD 1.96)	1.38 (SD 1.92)	1.17 (CI 95%: 0.98–1.40)	.0767	
	Related to CHF	0.48 (SD 1.04)	0.56 (SD 1.09)	1.52 (SD 1.05)	1.32 (CI 95%: 1.01–1.73)	.0411	

*Matched patients received a statistical weight: 1 for 1,943 matched intervention patients, 0.957 for 3,552 patients of the control group who were matched to two partners in the intervention group, and 1.914 for 167 control patients for whom only one matching partner could be identified.

[†]CHF is principal or secondary diagnosis of the hospitalization.

Table 3 shows the logistic regression model of survival after 1-year follow-up. The dichotomous outcome (survived/dead) was adjusted for the values of all matching criteria at baseline. Being in the intervention group increased the probability to survive significantly ($OR = 1.47, p = .0002$). Moreover, further determinates that were positive significantly associated with survival were female sex ($OR = 1.23, p = .020$), medication with angiotensin-converting enzyme inhibitors ($OR = 1.24, p = .013$), beta-blockers ($OR = 1.31, p = .002$) or AT1 receptor blockers ($1.84, p < .001$), or a diagnosis of neurotic, stress-related, and somatoform disorders (F40–F49, $OR = 1.36, p = .023$). In contrast, the following determinants were negatively associated with survival: living in a urban residential area ($OR = 0.72, p < .001$), older age ($OR = 0.96, p < .001$), higher number of hospitalizations related to CHF during the year before intervention ($OR = 0.86, p = .001$), medication with diuretics ($OR = 0.74, p = .002$) as well as a diagnosis of organic, including symptomatic, mental disorders (F00–F09, $OR = 0.51, p < .001$).

In addition, the probability of being alive after 1-year follow-up decreased with increasing age and NYHA class, except for patients with NYHA I. The matched dataset includes 48 patients with NYHA I (19 in intervention group and 29 in control group).

Table 4 shows the logistic regression model on survival after 2 years. The probability to survive was still significantly higher in the intervention group compared to the control group ($OR = 1.51, p < .001$). Determinants for survival were approximately the same as for the 1-year follow-up survival analysis with exception of the difference between NYHA classes I (reference) and II ($OR = 2.27, p = .010$) as an additional determinant.

Gender-Specific Survival

The interaction between study group and sex (completely adjusted logistic regression) was not significant neither after 1 ($p = .131$) nor after 2 years ($p = .508$). Nevertheless, we examined gender-specific survival results. The odds ratio for survival (completely adjusted logistic regression) after the first year for the female intervention subgroup is considerable greater ($OR = 1.75, CI 95\%: 1.29–2.38$) than for the male intervention group ($OR = 1.26, CI 95\%: 0.97–1.65$), both in relation to correspondent control groups. The difference between males and females is smaller after 2 years: $OR = 1.59$ for female subgroup, $OR = 1.43$ for male subgroup (Table 2).

Table 3: Logistic Regression Model Showing Survival after First Year (Intervention Group: $N = 1,922$, Control Group: $N = 3,680$)

	Reference	Odds Ratio	CI 95%		<i>p</i> -value
			2.5%	97.5%	
Study group	Control group	1.47	1.21	1.80	.0002
Residential area (Berlin vs. rural)	Rural	0.72	0.60	0.87	.0006
Age (in years)	(continuous)	0.96	0.95	0.97	<.0001
Sex	Male	1.23	1.03	1.46	.0197
NYHA class					
<i>NYHA II</i>	NYHA I	1.89	0.79	3.97	.1182
<i>NYHA III</i>	NYHA I	1.50	0.63	3.13	.3187
<i>NYHA IV</i>	NYHA I	1.06	0.44	2.23	.8787
CHF-related hospitalization	(continuous)	0.77	0.71	0.84	<.0001
Intake of medication related to CHF (yes/no by groups of agents)					
ACE inhibitors	No	1.24	1.05	1.48	.0133
Beta-blockers	No	1.31	1.11	1.56	.0016
Renin inhibitors	No	0.83	0.45	1.66	.5637
Glycosides	No	0.73	0.59	0.91	.0050
Diuretics	No	0.74	0.61	0.90	.0024
AT1 receptor blockers	No	1.84	1.44	2.38	<.0001
Mental and behavioral disorders (yes/no by blocks of ICD-10 Chapter V)					
F00–F09 (Organic, including symptomatic, mental disorders)	No	0.51	0.41	0.65	<.0001
F10–F19 (Mental and behavioral disorders due to psychoactive substance use)	No	0.83	0.62	1.13	.2323
F20–F29 (Schizophrenia, schizotypal, and delusional disorders)	No	1.09	0.47	3.02	.8567
F30–F39 (Mood [affective] disorders)	No	0.98	0.78	1.24	.8860
F40–F49 (Neurotic, stress-related, and somatoform disorders)	No	1.36	1.05	1.79	.0225
F50–F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	No	0.95	0.60	1.58	.8396
F60–F69 (Disorders of adult personality and behavior)	No	1.07	0.52	2.46	.8670
F70–F79 (Mental retardation)	No	0.50	0.19	1.61	.1988
F80–F89 (Disorders of psychological development)	No	—	—	—	—
F90–F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	No	1.29	0.23	26.28	.8136
F99–F99 (Unspecified mental disorders)	No	0.54	0.15	2.70	.3891
Intercept	—	193.58	64.16	630.67	<.0001

Table 4: Logistic Regression Model on Survival after 2-Year Follow-Up
(Intervention Group: $N = 1,827$, Control Group: $N = 3,507$)

	<i>Reference</i>	<i>Odds Ratio</i>	<i>CI95%</i>		
			2.5%	97.5%	<i>p-value</i>
Study group	Control group	1.51	1.28	1.77	<.0001
Residential area (Berlin vs. rural).	Rural	0.82	0.70	0.96	.0114
Age (in years)	(continuous)	0.95	0.94	0.96	<.0001
Sex	Male	1.18	1.03	1.36	.0197
NYHA class					
<i>NYHA II</i>	NYHA I	2.27	1.19	4.14	.0098
<i>NYHA III</i>	NYHA I	1.69	0.89	3.08	.0943
<i>NYHA IV</i>	NYHA I	1.23	0.64	2.24	.5217
CHF-related hospitalization	(Continuous)	0.75	0.70	0.81	<.0001
Intake of medication related to CHF (yes/no by groups of agents)					
ACE inhibitors	No	1.25	1.09	1.44	.0020
Beta-blockers	No	1.37	1.19	1.57	<.0001
Renin inhibitors	No	1.19	0.69	2.14	.5528
Glycosides	No	0.75	0.63	0.90	.0014
Diuretics	No	0.59	0.51	0.69	<.0001
AT1 receptor blockers	No	1.48	1.22	1.79	.0001
Mental and behavioral disorders (yes/no by blocks of ICD-10 Chapter V)					
F00–F09 (Organic, including symptomatic, mental disorders)	No	0.58	0.47	0.72	<.0001
F10–F19 (Mental and behavioral disorders due to psychoactive substance use)	No	0.72	0.57	0.92	.0081
F20–F29 (Schizophrenia, schizotypal, and delusional disorders)	No	1.41	0.66	3.32	.4031
F30–F39 (Mood [affective] disorders)	No	1.02	0.85	1.23	.8399
F40–F49 (Neurotic, stress-related, and somatoform disorders)	No	1.10	0.90	1.36	.3424
F50–F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	No	1.03	0.70	1.54	.8930
F60–F69 (Disorders of adult personality and behavior)	No	0.94	0.52	1.79	.8450
F70–F79 (Mental retardation)	No	0.96	0.35	3.11	.9373
F80–F89 (Disorders of psychological development)	No	—	—	—	—
F90–F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	No	1.30	0.33	8.90	.7428
F99–F99 (Unspecified mental disorders)	No	0.58	0.17	2.46	.4162
Intercept	—	122.76	50.43	308.19	<.0001

Hospitalization

The number of total hospital admissions per year amounted to 1.56 for the matched intervention group and 1.57 for the matched control group after the first year. Compared to the baseline number (2.54 and 2.53 per year, respectively), we observe a reduction in both groups. The number of CHF-related hospital admissions of both matched groups accounted to 0.61 per quarter year. Again, this is a reduction compared to the baseline number of 1.37 for both groups. Interestingly, we observed no further reduction during the second year, but rather a stable level of the number of hospital admissions for both groups.

Overall, weighted descriptive analyses revealed no remarkable group differences, neither with respect of follow-up time nor in type of hospitalization (all causes or CHF-related). Multivariable negative binomial regression suggested a slightly higher of total hospital admissions in the intervention group after 1 year compared to the control group (IRR = 1.01, CI 95 percent: 0.93–1.09, $p = .894$) and a higher number of CHF-related hospital admissions (IRR = 1.10, CI 95 percent: 0.98–1.23, $p = .093$).

The intervention group showed a greater number of total (IRR = 1.17, CI 95 percent: 0.98–1.40 $p = .077$) and CHF-related hospital admissions (IRR = 1.32, CI 95 percent: 1.01–1.73, $p = .041$) during the second year.

Sensitivity Analysis

In the sensitivity analysis, we assumed that all patients missing at follow-up died. If we fit regression models under this assumption according to our primary analysis, we observe lower, but still significant, odds ratios for survival after 1 year (OR = 1.42, CI 95 percent: 1.17–1.72, $p < .001$) and 2 years (OR = 1.40, CI 95 percent: 1.21–1.62, $p < .001$), respectively (results not shown).

Treated Analysis

Via propensity score matching, 1,381 intervention patients (thereof 56.1 percent male, mean age 73.8 years) and 2,678 control patients (thereof 56.1 percent male, mean age 73.8 years) were selected. The follow-up analysis after 1 year included information of 1,376 intervention patients (thereof 56.0 percent male) and 2,668 matched control patients (thereof 56.1 percent male).

The effects of the intervention for the treated group were larger than in the intention-to-treat analysis. In this analysis, compared to the control group the intervention group had a greater probability to survive 1 year (OR = 1.70, CI 95 percent: 1.31–2.21). Subgroup analyses stratified to men and women showed similar results for both sexes. For male intervention patients, the odds ratio for survival was 1.77 (CI 95 percent: 1.26–2.52) after 1 year. The odds ratio for survival for female intervention patients was 1.57 (CI 95 percent: 1.05–2.37) compared to the matched female control group.

DISCUSSION

AOK-Curaplan Herz Plus is a telemedicine program in a regular care setting for patients with a CHF diagnosis. Based on an analysis with routine data collected for reimbursement purposes, we could show that patients in the intervention program benefitted from this telemedicine intervention with regard to higher survival rates as compared to matched control patients. Beside sex, age, baseline number of CHF-related hospitalizations, and baseline health costs per quarter year, the place of residence of the patients (urban or rural) was a significant determinant for survival (with better survival for patients living in a rural area). There is no obvious explanation for this effect. There could be some selection effect, which cannot be further analyzed and explained because of the structure of the reimbursement data used.

To assess sensitivity, we calculated a Cox proportional hazards model to compare survival rates between the study arms using the same predictors as in the logistic model. The results (hazard ratio for study group (ref.: control group): 0.78; CI 95 percent: 0.69–0.88; $p < .001$) were consistent with the logistic model.

Our finding of an increased probability to survive for the intervention group as compared to appropriately matched controls was even more pronounced when the analyses were repeated for the treated population only (treated analysis). The findings were observed for both men and women. One-year survival rates were 88.0 percent for male and 90.3 percent for female intervention patients. In the treated intervention group, 775 of 1,381 patients (56.1 percent) were men. For patients of that group, 1-year survival rates were 92.0 percent for male and 92.5 percent for female intervention patients.

A Cochrane review on telephone support for patients with CHF summarized 25 studies and five published abstracts on structured telephone support

or telemonitoring programs and concluded that most of these programs were beneficial (Inglis et al. 2010).

Furthermore, survival benefits were found in the telephone-based structured monitoring HeartNetCare-HF (Angermann et al. 2012), in TEN-HMS (Cleland et al. 2005) and in a home-based telemanagement program with a portable device for measuring a one-lead ECG and additional nurses, available for teleconsultation (Giordano et al. 2009) and in The Whole System (Steventon et al. 2012).

Other studies determined no survival benefits. In TIM-HF (Telemedical Interventional Monitoring in Heart Failure), no significant improvement on mortality for the telemedicine management group could be shown (Koehler et al. 2011, 2012). No significant effect is present in a telephone-based interactive voice response system that collected daily information about symptoms and weight (Chaudhry et al. 2010). Although these studies are not directly comparable with the present study because of differences in setting, participating patients, and type and duration of the intervention, the results suggest that telemedicine interventions may have positive effects on survival, especially in studies with a longer duration of the intervention. Intervention studies are typically based on relatively small numbers of patients and a high intensity of the intervention, partially with active participation of hospitals. In contrast, our study is characterized by a low-threshold telemedicine intervention in an ambulant real care setting.

Our study suggests that women are more likely to benefit from the intervention in the first year. This effect is reduced in the second year. Differences exist between women and men in the syndrome of heart CHF with respect to risk factors (Regitz-Zagrosek and Lehmkuhl 2005), age of diagnosis, and prognosis (Regitz-Zagrosek et al. 2010). Adherence to guidelines in the diagnosis and treatment of CHF is less strict in women than in men, leading to undertreatment with medication (Johansson et al. 2015) and the underuse of expensive and invasive therapies (Regitz-Zagrosek and Lehmkuhl 2005). The participation in the program may improve the medical care, especially of the women.

We observed no remarkable differences in the number of hospital admissions per patient and year during follow-up time. Compared to baseline, the analysis revealed a reduction in the number of hospital admissions for both groups after 1 year. In the CHAMPION Trial, the treatment group had a significant 37 percent reduction in CHF hospitalization rates (Krahnke et al. 2015). The drop in readmissions for both intervention and control is remarkable. The early detection of decompensation may have caused patients to be

admitted to the hospital prior to worsening condition and thus had an impact on survival without reducing hospitalizations.

The impact on hospitalizations in other telemedicine interventions is variable (Inglis Sally et al. 2015; Kotb et al. 2015; Pandor et al. 2013a, b).

Strengths and Limitations

The AOK-Curaplan Herz Plus telemedicine program was conducted in a routine care setting. A broad range of patients was included with respect to age, degree of severity of CHF, and comorbidities. Also, formal exclusion criteria as the existence of mental health disorders and NYHA I and IV were not consequently adhered to by the recruiting general practitioners. On the other hand, this resulted in a typical group of patients and results might therefore be more likely to be transferable to the general population. Unfortunately, the proportion of patients that declined to participate in the program is unknown. If participants and nonparticipants systematically differed from the control group with respect to adherence, this could cause a bias.

The matching procedure is a trade-off between the similarity between the matched intervention and control group and the proportion of matched subjects of the total intervention group. Given the chosen matching algorithm, we could match 74.1 percent of the overall intervention group. Due to the large range of different comorbidities in this routine health care setting, it was not possible to match on a patient individual level for comorbidity directly. We assumed that patients with the same NYHA cause similar costs, and differences in cost classes probably reflect comorbidity. Therefore, we used the cost category as a proxy for comorbidity.

With the exception of diabetes, the prevalence of the comorbidities after the matching process was similar between the intervention and control group. However, the prevalence in the overall intervention group before matching was considerably lower. Hence, the prevalence of the comorbidities was balanced due to the matching process.

The matched groups are very similar at baseline. Nevertheless, there might be some selection bias. The matched intervention group tends to be older, overrepresented in the NYHA classes II and III, and related to lower health costs. This may limit the external validity of the analysis.

However, all patients in both groups had the same access to all providers of medical care. Therefore, it is unlikely that socioeconomic factors differentially between the groups influenced the kind or quality of care and, associated with that, the mortality rate.

Routine data of the statutory health insurance were available to perform the analysis. These data were primarily collected for reimbursement reasons. This means that the data may not always reflect real medical care.

Another problem was that data for some variables in this kind of datasets were only available if it is relevant for reimbursement. For example, if a patient did not see a doctor in some quarter year, no data about diagnoses were available in this quarter year. A limitation of the analysis is that some known independent predictors of our outcome (e.g., renal function or the presence of an implantable cardioverter-defibrillator) could not be included in the logistic regression model because these data were not available in the dataset of the statutory health insurance. The logistic models were calculated without adjusting for costs, because of a moderate correlation ($r = 0.40$) between hospitalizations and costs at baseline. Including costs at baseline in the model changes the results only slightly.

With respect to our analysis, we had to search for the NYHA class in quarter years prior to inclusion of the patients in many cases and, if available, used these as best imputations for the situation at the time of recruitment. A further limitation of using routine data was a lack of information about the dose and duration of the intervention.

Strength of our study was the completeness of the data and the sample size. By the combination of exact and propensity score matching algorithms, we achieved a high similarity between the groups in most variables. Despite the huge database from which the controls could be drawn, we could not identify two control patients for all intervention patients: two controls were found for 1,776 of 2,622 intervention patients (67.7 percent) and one control for 167 (6.4 percent) of the intervention patients. A total of 679 (25.9 percent) of the intervention patients could not be matched.

CONCLUSION

This evaluation shows that patients with CHF benefit from the telemedicine program AOK-Curaplan Herz Plus. The probability to survive is significantly increased in the intervention group (1- and 2-year follow-up). Results were even better for the intervention subgroup with documented start of treatment (treated group).

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.

RESEARCH ARTICLE

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Telemedical monitoring of patients with chronic heart failure has a positive effect on total health costs

Robert Herold¹, Wolfgang Hoffmann² and Neeltje van den Berg^{2*}

Abstract

Background: Telemedical programs for patients with chronic heart failure have shown inconsistent effects on survival and hospitalization. Few studies analyzed effects of telemedical interventions on health costs, although this outcome may determine whether or not a successful program will be adopted by health insurance providers. We evaluated a large sized telemedicine program provided by a German statutory health insurance, consisting of regular telephone contacts and, for a subgroup of the participants, provision of an electronic scale in a routine care setting. We examined the effects of the program on the total healthcare costs after one year compared to a matched control group.

Methods: The evaluation was based on reimbursement data of the statutory health insurance. Participants of the program were matched to appropriate controls using a combination of exact (e.g. 5-year age group, gender, NYHA class) and propensity score (e.g. medication, psychiatric comorbidity) matching.

The total health costs after one year were calculated on the basis of regression analyses in an intention-to-treat-approach. In a sensitivity analysis, the subgroup of patients with a documented beginning of the intervention was examined.

Results: Two thousand six hundred twenty two patients with chronic heart failure (55% male, mean age: 73.7 years) were included in the intervention program. 1943 participants (74%) could be matched with appropriate control patients. The telemedicine monitoring program for patients with chronic heart failure reduced total health costs after 12 months of the intervention: – 276€ per quarter year in rural regions and – 18€ in urban regions compared to the control group.

Conclusions: The telemedicine program could reduce total health costs, especially in rural regions in Germany.

Keywords: Chronic heart failure, Telemedical monitoring, Reimbursement data, Propensity score matching, Health costs

Background

Chronic heart failure (CHF) is a frequent cause of disability, emergency hospital admission and premature death [1, 2]. The prevalence and incidence rates of heart failure increase with age [3]. Due to demographic changes and the increasing probability to survive an acute myocardial infarction and diseases of the heart valves and the myocardium, the number of CHF-patients will continue to increase in the next years [4].

At the same time, chronic heart failure continues to be a fatal disease, with only 35% patients surviving 5 years

after the first diagnosis [3]. In 2002, German health insurance companies paid 2.3 times more for patients with than without CHF [5]. Total health costs of CHF in Germany were estimated at 2.9 billion€ in 2006 [6].

Telemedicine programs have been developed to improve monitoring and therapy of patients with chronic diseases [7]. Telemonitoring of patients with chronic heart failure can be used to detect early warning signs of impending decompensation and may be an effective strategy for disease management in high-risk heart failure patients to prevent hospitalizations and mortality [8].

Only a few studies examined the effect of telemedicine programs for CHF patients on total health costs. Systematic reviews report predominantly lower health costs for patients randomized to the intervention group [7–9]. A

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recent Cochrane review included 41 studies on structured telephone support or telemonitoring programs for patients with CHF. Four of fifteen studies that reported health cost analyses reported reductions in health costs, two studies reported increases in costs [7].

We evaluated the telemonitoring program “AOK-Curaplan Herz Plus” for patients with CHF, offered by a large statutory health insurance in Germany. The program comprised regular telephone coaching by special trained nurses in a telemedicine center, a modem-connected electronic scale in a subgroup of the patients, and the provision of information leaflets about coping with heart failure [10]. The primary outcome of this evaluation was total health costs per quarter year during the first year after enrolment into the intervention program for the entire intervention group (intention to treat analysis) compared to a matched control group. Secondary outcome was total health costs two years after enrolment. Further, a sensitivity analysis was conducted on total health costs per quarter year during the first year after enrolment in the subgroup of patients with a documented begin of the intervention (treated analysis).

Methods

Intervention program

AOK-Curaplan Herz Plus is a telemedicine program for patients suffering from CHF, offered by the statutory health insurance AOK Nordost in Germany. The program consists of regular telephone coaching and counseling, provision of information leaflets about disease-related themes, and a telemedical scale for weight monitoring. Telephone coaching and counseling is conducted by trained nurses in a telemedicine service center, specialized on medical services. Telephone contacts include feedback to conspicuous weight increase, talks to patient-individual topics and standard themes (e.g. diet, exercise, adherence to medication) [9]. Telephone contacts are conducted every 4 to 12 weeks, dependent on the patients' individual needs. If needed, patients can contact the telemedicine service center any time. In case of a deteriorating health situation, the nurses give concrete recommendations or contact the treating physician. The frequency of the telephone calls is individually tailored to each patient. The program is implemented in routine healthcare, additional to usual care, and has no defined duration. AOK-Curaplan Herz Plus started in 2006 and is still running in the German federal states of Berlin and Brandenburg.

Usual care for patients with CHF is based on German and international treatment guidelines.

Participants

The intervention was implemented in a regular care setting. Patients with a diagnosis of CHF (ICD-10 diagnosis

codes I50.12, I50.13 or I50.14 and NYHA class > I) with a high risk for a heart failure related hospitalization were informed about the program and invited to participate. High risk was defined as a prior heart-failure related hospitalization. Exclusion criterion was the presence of any diagnosed mental disorder at the time of recruitment. The recruitment of patients occurred during two phases: from 2006 to 2009, eligible patients were included by their treating general practitioners and cardiologists in private practices. Since 2009, eligible participants were retrieved from the database of the statutory health insurance AOK Nordost and were contacted directly by the health insurance company. All participating patients provided written informed consent.

Study design

To analyze the effect of the intervention on total health costs compared to an appropriate control group (intention-to-treat analysis), a quasi-experimental design was implemented [11].

Data from 2606 intervention patients and from 205,738 other patients fulfilling the inclusion criteria for the telemedicine program from the time period between the last quarter year of 2006 until the second quarter year of 2012 were retrieved from the database of the statutory health insurance. The data was on a patient-individual level, but completely anonymized, and, except for information about the federal state, without any regional data, so that it was not possible to re-identify single patients. The database included data to all matching variables and outcomes.

The control group was compiled using a combination of exact matching and propensity score matching (see section “matching” for further details). The control patients were retrieved from the total database of the statutory health insurance. For patients of the intervention group, the quarter year of enrollment served as baseline. Figure 1 shows the study design with baseline and follow-up analyses.

In a subsequent sensitivity analysis, the subgroup of patients with a documented start of the intervention was examined (treated analysis). Because of the highly variable time periods between recruitment and start of the intervention throughout the patient group, we conducted a separate matching procedure for the treated analysis using the quarter year of the start of the intervention as baseline quarter year.

Both matching procedures and statistical analyses were based on reimbursement data provided by the AOK Nordost. To analyze the effects of the intervention multivariate regression models were fitted including all matching variables and an array of potential confounders [12].

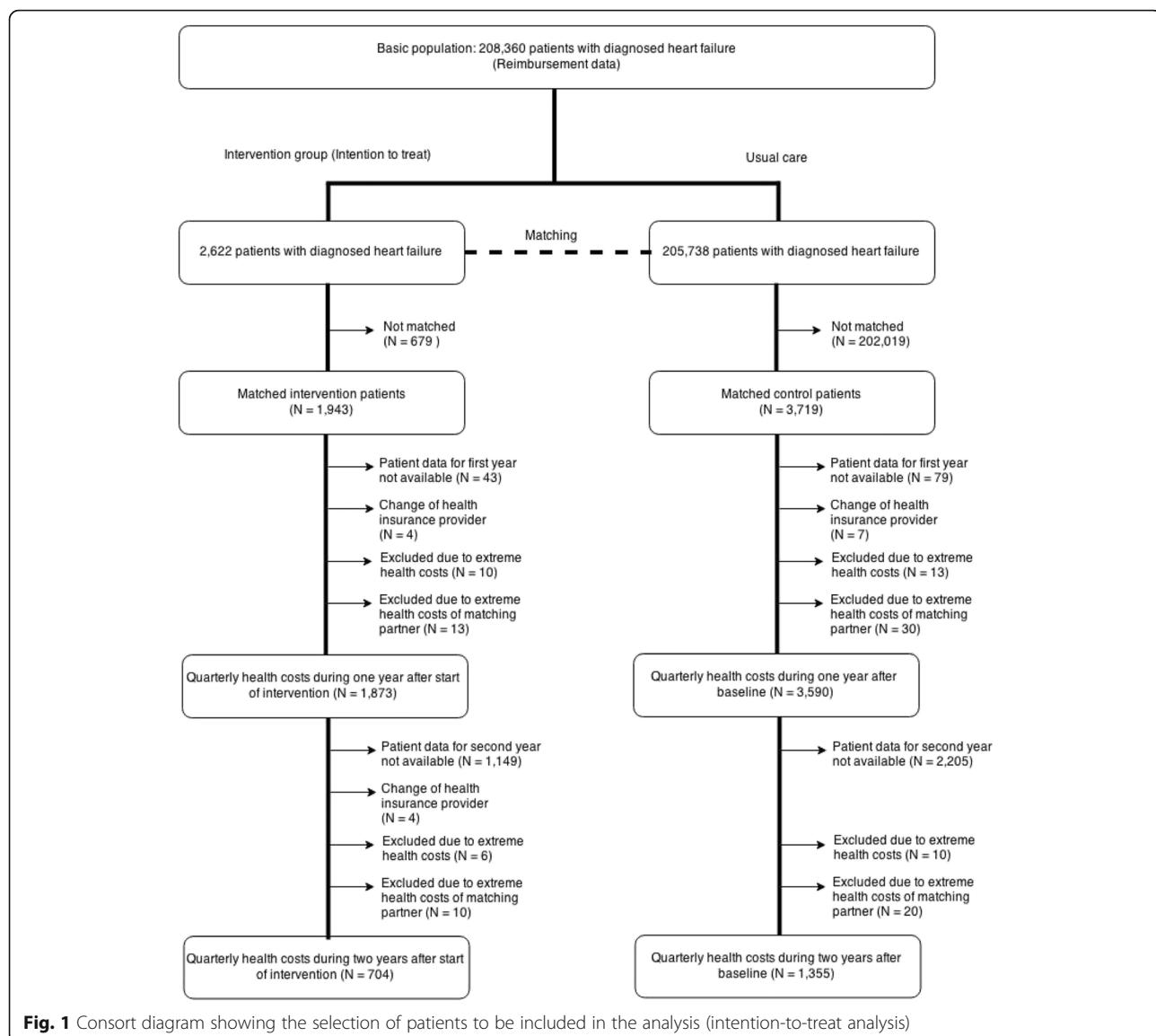


Fig. 1 Consort diagram showing the selection of patients to be included in the analysis (intention-to-treat analysis)

Matching procedure

The control group was retrieved from the total database of the statutory health insurance. The base population consisted of all patients with a diagnosis of chronic heart failure. We combined exact and propensity score matching using a nearest neighbor method (greedy algorithm) with restrictions in selected covariates (matching without replace, two controls per case at the maximum) [13].

Intervention patients were matched for their quarter year of enrolment (respectively, the quarter year of starting the intervention in the sensitivity analysis) and controls were drawn dynamically. Dynamically means that controls could be matched to an intervention patient every quarter year as long as they were insured, still alive and not matched in a prior quarter year to another intervention patient.

The following variables had to match exactly: sex, 5-year-age group, NYHA class, number of hospital admissions in the 12 months prior to enrolment, cost category (23 categories) and the presence of any mental or behavioral disorders (ICD-10: F00 – F99). Patients with missing information in any of these variables were excluded from the matching procedure. The following parameters were included as propensity score matching criteria: cardiovascular medication in 6 groups of active agents in the baseline quarter year (angiotensin-converting enzymes, beta-blockers, renin-inhibitors, cardiac glycosides, diuretics, and AT1 receptor blockers) and mental and behavioral disorders in 11 diagnoses groups in the baseline quarter year. Mental illness was considered as a disabling factor for successful program participation. However, a considerable number of patients with mental illness were

enrolled. Accordingly, mental disorders had to be included in the matching procedure.

Exclusion of extreme-cost-patients and capping of high costs

The statutory health insurance uses an algorithm to exclude patients with extreme costs and to cap costs exceeding a defined threshold in their internal analyses to prevent that single outliers bias the results. The underlying assumption is that very high costs are caused by events that are not associated with the disease (e.g. accidents). We followed this algorithm and excluded patients with health costs over 100,000€ per year. Matching partners of high cost patients were also excluded. Additionally, in all remaining patients, inpatient health costs were capped to a maximum of 20,000€ per year, costs for home health care to 15,000€ per year and medication costs to 7000€ per year.

Statistical analysis

The primary analysis was an intention-to-treat analysis which included all matched patients. After matching, all matched patients received a statistical weight to account for the fact, that for some patients only one matching partner could be assigned (1 for 1943 matched intervention patients, 0.957 for 3552 patients of the control group who were matched to two partners in the intervention group and 1.914 for 167 control patients for whom only one matching partner could be identified).

In the baseline analysis, group differences in continuous variables were compared using the t-test, the chi-square test was used to compare categorical variables.

Primary endpoint of the analysis was the average of the total health costs over the four quarter years of the first year after recruitment. If patients survived less than four quarter years after baseline, we calculated the average of the quarter years when patients were still alive. The analysis of the two-year follow-up proceeded the same way with a maximum of eight quarter years.

The analyses were conducted using multivariate linear regression models. All models were adjusted by all baseline matching variables and by the residential area of the patients (dichotomized as Berlin (= urban) and other (= rural)). An interaction term "study group x residential area" was included in the models because bivariate analyses indicated an effect modification of the intervention of the place of residence on the total health costs.

We considered a *p*-value < 0.05 statistically significant in all comparisons.

Statistics were calculated using R statistical software, version 3.0.0 (R Foundation for Statistical Computing, Vienna, Austria). We used the R packages "MatchIt" [14] for data matching, "survey" [15] for weighted descriptive analyses, and "stats" [16] for regression models.

Results

Intention-to-treat analysis

Patients were excluded from the regression analyses for the following reasons: 1) missing follow up data (health cost data were available until the fourth quarter year of 2011), 2) patients changed their health insurance company during follow-up time, 3) extreme health costs above 100,000€/year either of a patient (see methods for details) (Fig. 1).

Matching

One thousand nine hundred forty three intervention patients (74% of the patients in the intervention group) could be matched to 3719 control patients. Most frequent cause of failing matching was missing information about the NYHA-class (60% of the 679 not matched intervention patients).

Baseline characteristics

Table 1 shows the distribution of parameter-values for the quarter year of enrolment in the intervention program for patients of the intervention group, and the quarter year of matching for patients of the control group (baseline quarter year). 54% of the patients in both groups were males; the mean age was 74.4 years. NYHA II and III were the most frequent NYHA classes. The total health costs per quarter year in the year prior to the baseline quarter year averaged 3747€ (SD: 3007€) in the intervention group and 3750€ (SD: 3021€) in the control group. 743 patients of the intervention group (38%) had at least one diagnosed mental disorder (ICD-10 Chapter V) in the baseline quarter year.

Intervention and control group were similar in most variables. Significant differences concerned the medication with AT1 receptor blockers, the number of emergency hospitalizations, the residential area, the level of care, and the proportion of patients living in a nursing home.

One-year follow-up

Figure 1 shows the flowchart of the analysis; 5433 of 5662 patients could be included in the one-year-follow-up analysis. The processed mean average quarterly health costs in the first year following the recruitment the total health care costs differ by 8€ overall between the intervention (2921€) and control (2929€) groups. Comparing the health costs of various subgroups of patients reveals considerable differences. As expected, costs are much higher in the group of patients who died in the year after recruitment. Rural patients caused lower health costs in both groups compared to the patients in Berlin. The crude difference between intervention and control patients was - 64€ in Berlin and - 259€ in rural regions, indicating effect modification which needed to be appropriately addressed in the fully adjusted model. Average health costs in the first year after

Table 1 Baseline characteristics of the intervention patients and controls

Variable	Mean (SD) / N (%)		Test statistics	
	Intervention group (N = 1943)	Control group (N = 3719)		
Sex				
Male	1052 (54.14%)	2014 (54.15%)	–	
Female	891 (45.86%)	1705 (45.85%)	–	
Age groups				
41–45 years	8 (0.41%)	15 (0.41%)	–	
46–50 years	22 (1.13%)	42 (1.12%)	–	
51–55 years	46 (2.37%)	88 (2.36%)	–	
56–60 years	69 (3.55%)	132 (3.54%)	–	
61–65 years	127 (6.54%)	243 (6.52%)	–	
66–70 years	305 (15.70%)	585 (15.72%)	–	
71–75 years	426 (21.92%)	816 (21.93%)	–	
76–80 years	441 (22.70%)	845 (22.73%)	–	
81–85 years	314 (16.16%)	601 (16.16%)	–	
86–90 years	159 (8.18%)	304 (8.18%)	–	
91–95 years	26 (1.34%)	49 (1.33%)	–	
Mean age [years]	74.44 (SD 8.97)	74.48 (SD 9.04)	t = –0.125, p = 0.9004	
NYHA class				
NYHA I	19 (0.98%)	36 (0.98%)	–	
NYHA II	614 (31.60%)	1175 (31.60%)	–	
NYHA III	779 (40.09%)	1491 (40.09%)	–	
NYHA IV	531 (27.33%)	1016 (27.33%)	–	
Hospital admissions (baseline year)	All causes	2.54 (SD 1.73)	2.53 (SD 1.88)	t = 0.090, p = 0.9283
Emergency hospitalization (baseline year)	All causes	0.65 (SD 1.27)	0.55 (SD 1.30)	t = 2.752, p = 0.0059**
Total health costs [€] (quarterly mean in baseline year, SD)	All regions	3747 (3007)	3750 (3021)	t = –0.037, p = 0.9705
	Urban	3723 (2900)	3959 (3503)	t = –1.555, p = 0.1201
	Rural	3820 (3313)	3677 (2829)	t = 0.882, p = 0.3777
Health cost [€] (mean, SD)	In-patient	2464 (2376)	2403 (2322)	t = 0.896, p = 0.3702
	Outpatient	296 (635)	294 (764)	t = 0.126, p = 0.9000
	Drugs	547 (788)	564 (751)	t = –0.752, p = 0.4523
	Remedy	49 (131)	39 (126)	t = 2.705, p = 0.0068**
	Adjuvant	97 (213)	110 (226)	t = –2.100, p = 0.0358*
	Home health care	127 (525)	140.06 (426)	t = –0.919, p = 0.3583
	Travel costs	160 (271)	198 (304)	t = –4.660, p < 0.0001***
	Rehabilitation	7 (44)	3 (27)	t = 3.738, p = 0.0002***
Medication (percentage “yes” per active agent in baseline quarter)	Angiotensin-converting enzymes	845 (43.49%)	1637 (44.01%)	Chi ² = 0.119, p = 0.7301
	Beta-blockers	1261 (64.90%)	2340 (62.93%)	Chi ² = 2.057, p = 0.1515
	Renin-inhibitors	36 (1.85%)	51 (1.36%)	Chi ² = 1.754, p = 0.1853
	Cardiac glycosides	279 (14.36%)	548 (14.73%)	Chi ² = 0.111, p = 0.7388
	Diuretics	1298 (66.80%)	2507 (67.40%)	Chi ² = 0.178, p = 0.6727
	AT1 receptor blocker	385 (19.81%)	651 (17.51%)	Chi ² = 4.397, p = 0.0360*

Table 1 Baseline characteristics of the intervention patients and controls (Continued)

Variable		Mean (SD) / N (%)		Test statistics
		Intervention group (N = 1943)	Control group (N = 3719)	
Mental and behavioral disorders	Yes	743 (38.24%)	1421 (38.20%)	–
disorders (baseline quarter)	No	1200 (61.76%)	2298 (61.80%)	
Residential Area	Berlin	1461 (75.19%)	969 (26.06%)	$\chi^2 = 1411.6, p < 0.0001^{***}$
	Brandenburg	436 (22.44%)	1482 (39.84%)	
	Mecklenburg-Western Pomerania	27 (1.39%)	1235 (33.20%)	
	Other	19 (0.98%)	34 (0.90%)	
Nursing care level of care ^a	No care	1398 (71.95%)	2678 (72.02%)	$\chi^2 = 20.932, p = 0.0001^{***}$
	Level 1	376 (19.35%)	615 (16.53%)	
	Level 2	159 (8.18%)	370 (9.94%)	
	Level 3	10 (0.51%)	56 (1.52%)	
Living in nursing home	Yes	159 (8.18%)	498 (13.39%)	$\chi^2 = 33.182, p < 0.0001^{***}$
	No	1784 (91.82%)	3221 (86.61%)	

^aStandardized classification of the level of nursing care in Germany. Significance codes: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

baseline were broken down to cost segments. Inpatient costs contribute the largest part of the total health costs in both groups (Table 2).

To represent the modification of the intervention effect by place of residence of the patients (urban or rural) we added the interaction term “study group x residential area” into the regression model. Table 3

shows the regression model for total health costs in the first year of follow up. This model was adjusted for all matching variables, the patients’ residential area and the interaction between study group and residential area. Statistically significant determinants for lower health costs were the intake of a beta-blocker ($p = 0.0014$). Significant predictors for higher health costs were

Table 2 Unadjusted subgroup means of processed^a quarterly health costs in the first year after baseline^b

	Intervention group		Control group	
	Mean (CI 95%)	N	Mean (CI 95%)	N
All Patients	€ 2921 (2773–3068)	1873	€ 2929 (2816–3041)	3590
Survived first year	€ 2397 (2279–2515)	1670	€ 2417 (2320–2514)	3105
Died	€ 7229 (6509–7948)	203	€ 6176 (5728–6625)	485
Male	€ 2941 (2740–3142)	1004	€ 3013 (2854–3172)	1925
Female	€ 2897 (2679–3115)	869	€ 2830 (2673–2987)	1665
Urban (Berlin)	€ 3023 (2845–3200)	1405	€ 3086 (2844–3329)	930
Rural	€ 2615 (2360–2869)	468	€ 2873 (2748–2999)	2660
Total health costs	€ 2921 (2773–3068)	1873	€ 2929 (2816–3041)	3590
Inpatient	€ 1557 (1441–1673)	1873	€ 1500 (1419–1580)	3590
Outpatient	€ 364 (322–405)	1873	€ 346 (309–382)	3590
Drugs	€ 508 (487–529)	1873	€ 531 (515–547)	3590
Remedy	€ 57 (50–63)	1873	€ 47 (42–51)	3590
Adjuvant	€ 115 (104–126)	1873	€ 133 (124–142)	3590
Home health care	€ 155 (134–176)	1873	€ 179 (163–194)	3590
Travel costs	€ 160 (142–178)	1873	€ 193 (176–209)	3590
Rehabilitation	€ 5 (3–6)	1873	€ 2 (1–3)	3590

^aHealth costs after performing the excluding-and-capping algorithm

^bMaximally 4 quarter years, less for patients who died within first year

Table 3 Results of regression analysis of processed^a quarterly health costs in first year after baseline (N = 5463)

	Reference	Estimate [in €]	CI 95% 2.5%	CI 95% 97.5%	P-value
Study group	Control group	-276.04	-573.18	21.10	0.0686
Residential area (Berlin vs. rural)	Rural	180.81	-49.03	410.65	0.1231
Interaction: Group x Residential area		257.77	-131.35	646.90	0.1941
Age group					
46–50 years	41–45 years	878.30	-652.97	2409.58	0.2609
51–55 years	41–45 years	669.75	-749.92	2089.43	0.3551
56–60 years	41–45 years	641.50	-743.15	2026.14	0.3638
61–65 years	41–45 years	448.94	-905.54	1803.43	0.5159
66–70 years	41–45 years	828.90	-502.34	2160.14	0.2223
71–75 years	41–45 years	1117.78	-210.13	2445.69	0.0990
76–80 years	41–45 years	1160.55	-167.31	2488.41	0.0867
81–85 years	41–45 years	973.17	-359.70	2306.04	0.1524
86–90 years	41–45 years	876.95	-471.87	2225.77	0.2025
91–95 years	41–45 years	1168.45	-340.20	2677.11	0.1290
Sex	Male	-73.85	-245.19	97.49	0.3982
NYHA class					
NYHA II	NYHA I	18.38	-793.15	829.91	0.9646
NYHA III	NYHA I	210.53	-600.60	1021.65	0.6109
NYHA IV	NYHA I	398.18	-419.09	1215.45	0.3396
Hospitalizations related to CHF	(continuous)	52.03	-51.72	155.79	0.3256
Baseline health costs	(continuous)	0.37	0.34	0.40	< 0.0001***
Intake of medication related to CHF (yes / no by groups of agents)					
Angiotensin-converting enzyme	no	-139.92	-313.52	33.69	0.1142
Beta-blocker	no	-279.06	-450.13	-107.98	0.0014**
Renin-inhibitors	no	-75.07	-734.15	584.01	0.8233
Cardiac glycosides	no	147.81	-81.40	377.01	0.2062
Diuretics	no	394.65	214.89	574.40	< 0.0001***
AT1 receptor blocker	no	-25.55	-247.64	196.54	0.8216
Mental and behavioral disorders (yes / no by blocks of ICD-10 Chapter V)					
F00 – F09 (Organic, including symptomatic, mental disorders)	no	465.72	173.79	757.65	0.0018**
F10 – F19 (Mental and behavioral disorders due to psychoactive substance use)	no	39.64	-257.67	336.94	0.7938
F20 – F29 (Schizophrenia, schizotypal and delusional disorders)	no	-34.52	-936.45	867.41	0.9402
F30 – F39 (Mood [affective] disorders)	no	109.85	-120.77	340.48	0.3504
F40 – F49 (Neurotic, stress-related and somatoform disorders)	no	51.25	-188.92	291.42	0.6757
F50 – F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	no	343.92	-130.81	818.64	0.1556
F60 – F69 (Disorders of adult personality and behavior)	no	-120.35	-859.94	619.25	0.7497
F70 – F79 (Mental retardation)	no	321.91	-921.90	1565.71	0.6119
F80 – F89 (Disorders of psychological development)	no	-	-	-	-
F90 – F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	no	612.00	-991.08	2215.09	0.4542
F99 – F99 (Unspecified mental disorders)	no	490.90	-1333.73	2315.52	0.5979
Intercept	-	249.86	-1318.15	1817.88	0.7548

^aHealth costs after performing the excluding-and-capping algorithm, Significance codes: ***p < 0.001, **p < 0.01, *p < 0.05

higher baseline health costs ($p < 0.0001$), the intake of diuretics ($p < 0.0001$) a diagnosis in the group of organic, mental disorders (F00 – F09, $p = 0.0018$).

Compared to the matched controls, total health costs in the first year after baseline were lower in the intervention group. The difference between both groups was – 276€ in rural regions and – 18€. Neither the parameters for the study group nor for the residential area and the interaction between them were statistically significant.

Two-year follow-up

Table 4 shows the regression model for the two-year follow up (sensitivity analysis planned a priori). The model was adjusted for the same parameters as the model for the one-year-follow up. Statistically significant determinant for lower health costs was the intake of beta blockers ($p = 0.0007$). Higher baseline health costs ($p < 0.0001$) and the intake of diuretics ($p = 0.0003$) were significant determinants for higher health costs. The intervention group showed lower health costs in rural regions (– 299€ per quarter year) but higher health costs in Berlin (+ 109€, compound effect of study group (– 299€) and interaction of group and residential area (+ 407€)) compared to the control group.

Sensitivity analysis (treated patients)

In a sensitivity analysis, the total health costs per quarter year of patients with a documented start of treatment were compared to a separately matched control group. Here, only the one-year follow-up was analyzed because data of a large part of the participants were not available for two-year follow-up. The intervention group showed lower health costs in rural regions (– 551€ per quarter year) and in urban regions (– 267€, compound effect of study group (– 551€) and interaction of group and residential area (+ 284€)) as well.

Discussion

In an analysis based on routine data, collected for reimbursement purposes, it was shown that the total health costs for intervention patients after one year were lower compared to a control group that had been matched for a large array of variables. Beside age, NYHA-class and baseline health costs, somewhat unexpectedly, the place of residence of the participating patients (urban or rural) was an important determinant for the development of the health costs over time (generally with better development for patients with a rural place of residence). A possible cause could be the higher availability of health care services in urban areas that tend to be more cost-intensive at the same time.

In addition to the intention-to-treat analysis, we performed a treated analysis with patients for which the beginning of the intervention was positively documented.

The results of the treated analysis support the findings of the more conservative intention-to-treat approach.

Hendricks et al. analyzed inpatient treatment costs of 1202 patients participating in a telemedicine monitoring program from a large German statutory health insurance company. The follow-up time was 54 months. The average annual costs for CHF related inpatient treatment in the intervention group were significantly lower than the equivalent costs in the control group (684€ per patient, Mann-Whitney-U-Test: $p < 0.0001$). Both groups show no significant differences in respect of number of hospital days and average costs per hospital stay [17].

In a prospective study on inpatient costs, 502 patients were randomized into an intervention and a control group. The intervention consisted of the monitoring of the body weight of the participants during one year. After an average observation period of 12 months, the annual hospital costs were reduced by 7128€ per patient while annual drug expenditure had increased by 245€ per patient (not significant). The total treatment costs had decreased by 6993€ per patient ($p = 0.05$). Reported savings are much greater compared to our results. But unfortunately, the authors don't adjust the results for baseline differences [18].

Neumann et al. evaluated the results of the HeartNetCare-HF (HNC) study (Würzburg / Germany). The overall costs per person were 3535€ in the HNC intervention group ($n = 352$) and 3038€ in the usual group ($n = 363$) within six months (p value for difference: 0.10). The HNC group showed a reduced risk of all-cause death (9% vs. 14%, $p = 0.03$). The authors state a positive cost-effectiveness (the ratio between the difference in costs and the difference in all-cause mortality) since HNC accounted for 8284€ per death avoided within the 6 months [19].

Zertiva is a telemedicine program for patients with CHF, offered by the statutory health insurance "Techniker Krankenkasse". 164 Patients were included after they had been hospitalized due to CHF; the follow-up period was 180 days. The standard care cohort was retrieved from routine data. The telemedicine group showed lower total health costs after 180 days compared to the matched controls (2292€ per patient and 3746€, respectively). Effectiveness adjusted health costs (total health costs divided by "success rate", meaning no hospitalization due to CHF during follow-up period) accounted for 3065€ for the telemedicine group and 6397€ for the control group, respectively [20].

In a retrospective analysis, conducted on the basis of data from 2009 until 2013 of a comprehensive telehealth program (existing of the transmission of vital data, daily telephone coaching, and continuous decision-making support) the cost data of 575 patients with chronic cardiovascular diseases were compared to the data of 1178

Table 4 Results of regression analysis of processed^a quarterly health costs in first two years after baseline (N = 2059)

	Reference	Estimate	CI 95%		p-value
			2.5%	97.5%	
Study group	Control group	-298.58	-1312.13	714.97	0.5635
Residential area (Berlin vs rural)	Rural	262.69	-101.60	626.98	0.1575
Interaction: Group x Residential area		407.35	407.35	1493.06	0.4619
Age group					
46–50 years	41–45 years	2832.23	-782.80	6447.27	0.1246
51–55 years	41–45 years	2875.11	-606.67	6356.89	0.1055
56–60 years	41–45 years	2600.31	-823.07	6023.69	0.1365
61–65 years	41–45 years	2569.53	-820.65	5959.71	0.1373
66–70 years	41–45 years	2840.77	-533.57	6215.11	0.0989
71–75 years	41–45 years	3259.24	-109.66	6628.14	0.0579
76–80 years	41–45 years	3318.69	-50.93	6688.32	0.0536
81–85 years	41–45 years	3017.17	-356.79	6391.14	0.0796
86–90 years	41–45 years	2919.52	-469.23	6308.27	0.0913
91–95 years	41–45 years	2870.68	-689.65	6431.00	0.1140
Sex	Male	-96.52	-369.46	176.42	0.4881
NYHA class					
NYHA II	NYHA I	314.97	-757.31	1387.24	0.5646
NYHA III	NYHA I	375.11	-696.74	1446.96	0.4926
NYHA IV	NYHA I	776.31	-302.57	1855.18	0.1584
Hospitalizations related to CHF	(continuous)	-27.61	-195.63	140.40	0.7472
Baseline health costs	(continuous)	0.34	0.29	0.39	< 0.0001***
Intake of medication related to CHF (yes / no by groups of agents)					
Angiotensin-converting enzyme	no	-251.08	-520.92	18.76	0.0682
Beta-blocker	no	-470.81	-741.91	-199.71	0.0007***
Renin-inhibitors	no	-283.79	-1553.61	986.03	0.6612
Cardiac glycosides	no	97.57	-252.61	447.75	0.5848
Diuretics	no	533.86	247.94	819.78	0.0003***
AT1 receptor blocker	no	-140.25	-491.33	210.83	0.4335
Mental and behavioral disorders (yes / no by blocks of ICD-10 Chapter V)					
F00 – F09 (Organic, including symptomatic, mental disorders)	no	386.31	-87.09	859.70	0.1097
F10 – F19 (Mental and behavioral disorders due to psychoactive substance use)	no	-83.55	-544.49	377.39	0.7223
F20 – F29 (Schizophrenia, schizotypal and delusional disorders)	no	-288.83	-1375.19	797.53	0.6021
F30 – F39 (Mood [affective] disorders)	no	30.78	-326.67	388.23	0.8659
F40 – F49 (Neurotic, stress-related and somatoform disorders)	no	11.66	-351.60	374.92	0.9498
F50 – F59 (Behavioral syndromes associated with physiological disturbances and physical factors)	no	-86.95	-775.45	601.54	0.8044
F60 – F69 (Disorders of adult personality and behavior)	no	816.43	-367.37	2000.23	0.1764
F70 – F79 (Mental retardation)	no	291.70	-2155.13	2738.54	0.8152
F80 – F89 (Disorders of psychological development)	no	-	-	-	-
F90 – F98 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence)	no	-340.42	-2933.64	2252.80	0.7969
F99 – F99 (Unspecified mental disorders)	no	5878.45	-562.31	12,319.21	0.0736
Intercept	-	-1689.37	-5226.05	1847.32	0.3490

^aHealth costs after performing the excluding-and-capping algorithm, Significance codes: ***p < 0.001, **p < 0.01, *p < 0.05

matched patients. The monthly average medical costs were US\$588 (SD 1498) in the telehealth group and US\$1164 (SD 3037) in the matched control group ($p = 0.02$) [21]. This study was conducted in Taiwan and results might less comparable to our study.

In many studies on telemonitoring for CHF patients, survival and the number of hospitalizations are endpoints. The effects of telemonitoring on health costs have been analyzed only in few studies. Often, only inpatient health costs instead of total health costs were considered as endpoint. Previous studies differ in design (randomized controlled design vs. use of routine data for comparison), average age, NYHA stage at baseline, and follow-up time. However, in most previous studies intervention groups tend to show reductions in health costs. Compared to our intervention patients, other study groups tend to be younger at baseline, have a lower NYHA class and have a lower number of participants. Moreover, other settings tend to be more specific, included patients seem to less heterogeneous and therefore less reflecting the total group of patients.

Strengths and limitations

A strength of this study is the large number of participating patients and its closeness to regular health care. All data used for the analysis were retrieved from original reimbursement data. Hence, there was no systematic difference in the data structure or data assessment between the patients in the intervention, and in the control group. The documentation of total direct health costs was complete and valid comparisons could be calculated. Since the intervention was conducted in a routine care setting, the results are likely transferable to the entire non-institutionalized CHF population of this statutory health insurance.

The study has several limitations. By applying propensity score matching we can only approximate the advantages of randomized trials. Data on social demographic variables were not available and despite a comprehensive two step matching process some residual confounding may have persisted due to unobserved variables. We could only match patients whose latest diagnose of NYHA class was within the timeframe of the available data (but before the date of matching).

A large part of the patients did not meet the inclusion and exclusion criteria because they had a diagnosed mental disorder at baseline. Possible causes were 1) participating cardiologists were not aware of diagnoses of mental disorders with their patients, 2) exact dates of diagnoses are not available in the data base, the data is stored on the basis of quarter years, and 3) data is reported retrospectively by the providers of medical services.

The large number of patients with mental disorders may have had an influence on the effect size of the

intervention. On the other hand, including patients with mental disorders meets the real composition of the patient group and increases the external validity of the results.

The follow-up time is relatively short. Results might be inflated [22, 23] since long term effects like regression to the mean could not be analyzed. Interventions to maintain good adherence for long-term lifestyle changes can be very challenging [24]. The health insurance could not provide information on the number of telephone contacts per patient. As part of the program some patients had received additional services (such as provision of a modem-connected scale), but this was unknown for the individual patients. Finally, only data of one health insurance were available, therefore the results can only be representative for the member population of this statutory health insurance, not for the entirety of CHF patients.

Implications of telemonitoring programs for the treatment of CHF patients

The analysis of the telemonitoring program of the AOK Nordost and the results of other programs show that telemonitoring programs do not increase costs of treatment. This opens good opportunities to integrate telemonitoring programs in the treatment and monitoring of patients with CHF. Especially in rural regions with large distances to providers of medical services, this kind of intervention can ensure or improve the quality of healthcare.

Conclusions

The AOK-Curaplan Herz Plus program reduced short-term health costs, especially in rural regions. The sensitivity analysis (treated approach) shows larger effects which is an indication that the effects do really originate from the telemedicine intervention and that the true impact might be larger than observed in the primary intention-to-treat-analysis.

Abbreviations

CHF: Chronic heart failure; HNC: HeartNetCare-Heart Failure Study;
NYHA: New York Heart Association

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Availability of data and materials

The data were supplied by the AOK Nordost for this project only. It is not allowed to make these data publicly available.

Authors' contributions

RH, WH and NvdB designed the study. RH performed the statistical analyses. RH, WH and NvdB interpreted the results. RH wrote the manuscript. All authors read and approved the manuscript.

Ethics approval and consent to participate

Not applicable. Only de-identified health insurance data were used in this study. The statutory health insurance AOK Nordost supplied completely de-identified data and gave us permission to analyze the data in this project and to publish the results in aggregated form.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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