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Effect of a Quality Improvement Intervention for Acute Heart Failure in South India: An Interrupted Time Series Study

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On behalf of all Co-Authors, the corresponding Author shall bear full responsibility for the submission. Any changes to the list of authors, including changes in order, additions or removals will require the submission of a new author agreement form approved and signed by all the original and added submitting authors.

This statement is to certify that all authors have seen and approved the manuscript being submitted, have contributed significantly to the work, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to the *International Journal of Cardiology.*

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Abstract

Background—Although quality improvement interventions for acute heart failure have been studied in high-income countries, none have been studied in low- or middle-income country settings where quality of care can be lower. We evaluated the effect of a quality improvement toolkit on process of care measures and clinical outcomes in patients hospitalized for acute heart failure in 8 hospitals in Kerala, India utilizing an interrupted time series design from February 2018 to August 2018.

Methods—The quality improvement toolkit included checklists, audit-and-feedback reports, and patient education materials. The primary outcome was rate of discharge guideline-directed medical therapy for patients with heart failure with reduced ejection fraction. We used mixed effect logistic regression and interrupted time series models for analysis.

Results—Among 1400 participants, mean (SD) age was 66.6 (12.2) years, and 38% were female. Mean (SD) left ventricular ejection fraction was 35.2% (9.7%). The primary outcome was observed in 41.3% of participants in the intervention period and 28.1% of participants in the control period (difference 13.2%; 95% CI 6.8, 19.0; adjusted OR = 1.70; 95% CI 1.17, 2.48). Interrupted time series model demonstrated highest rate of guideline-directed medical therapy at discharge in the initial weeks following intervention delivery with a concomitant decline over time. Improvements were observed in discharge process of care measures, including diet counseling, weight monitoring instructions, and scheduling of outpatient clinic follow-up but not hospital length of stay nor inpatient mortality.

Conclusions—Higher rates of guideline-directed medical therapy at discharge were observed in Kerala. Broader implementation of this quality improvement intervention may improve heart failure care in low- and middle-income countries.

Summary Tweet: QI toolkit in Kerala, India shows improvements in GDMT at discharge for patients with HFrEF. Centre for Chronic Disease Control, Cardiological Society of India, @DukeGHI, @Fogarty_NIH, @NMCardioVasc, @FSMGlobalHealth

Keywords

Heart failure; Quality improvement; India

Introduction

The burden of heart failure (HF) is increasing worldwide and has disproportionately shifted toward low- and middle-income countries due to population growth, aging, and a greater prevalence of major heart failure risk factors, including hypertension, diabetes, and ischemic heart disease.[1–3] The outcomes of HF patients in low- and middle-income countries remain poor, with inpatient mortality rates around 8% (95% CI: 6% to 10%), which are almost triple

to some high-income country groups.[4–6] Almost 50% of participants died at 3 years in the vanguard HF registry in India, reaching mortality rates observed much later in high-income country settings.[7,8] Improvements in HF mortality in high-income countries over time have been attributed to increased adherence to guideline-directed medical and device therapy which is a key heart failure performance measure.[9,10] Despite high-quality evidence that guideline-directed medical therapy reduces morbidity and mortality of patients with heart failure with reduced ejection fraction (HFrEF), only 25% of patients were discharged on guideline-directed medical therapy in the Trivandrum Heart Failure Registry in Kerala, India revealing a potential target for intervention.[5]

Improving the quality and safety of health systems, which are increasingly recognized as key strategies for improving clinical outcomes, is a global health priority.[11,12] Quality improvement initiatives have been developed in high-income countries to improve health system quality and subsequent clinical outcomes in patients with HF with limited effect, but none have been studied in low- or middle-income countries where there is a greater potential effect in the setting of lower baseline quality of care.[4,13] Most quality improvement research in India has been focused on acute coronary syndrome care, and HF remains understudied despite the potential to improve clinical outcomes and population health.[14,15] To fill this gap, we developed, implemented, and evaluated a locally-contextualized HF quality improvement toolkit-based intervention compared to usual care for patients with acute HF in 8 hospitals in Kerala, India using an interrupted time series study design.[16]

Methods

Study design

The Heart Failure Quality Improvement in Kerala (HF QUIK) study was a quasi-experimental study evaluating the effect of a locally-contextualized quality improvement toolkit on process of care measures and clinical outcomes in patients hospitalized for acute HF in 8 hospitals in Kerala, India from February 2018 to August 2018. The study utilized an interrupted time series study design. The pre-intervention period was from February 5th 2018 to May 6th 2018, and the post-intervention period was from May 6th 2018 to August 5th 2018. All data were entered online by study coordinators at each site using a Health Insurance Portability and Accountability Act (HIPAA)-compliant electronic data capture tool (REDCap, Vanderbilt University, Nashville, TN, USA).[17]

The study protocol was reviewed by and received ethics board approval from Duke University (Durham, NC, USA), Centre for Chronic Disease Control (New Delhi, Delhi, India), Cardiological Society of India-Kerala Chapter (Kochi, Kerala, India) and Indian Health Ministry Screening Committee (New Delhi, Delhi, India) in November 2017. No changes were made to the study protocol during the course of the study. Because data were used at the local hospitals for the purpose of quality improvement, sites were granted a waiver of informed consent under the Common Rule.

Hospitals and study participants

We purposively recruited 8 hospitals in Kerala, India from a sampling frame of hospitals (n = 63) that had previously participated in the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) trial.[15] All hospitals that were approached participated in the study. Hospitals varied in region and type, including government, non-profit/charity, and private hospitals to capture a range of implementation settings. Hospitals enrolled consecutive patients with a primary admission diagnosis of acute HF. Patients were eligible for inclusion if they were adults aged 18 years or older and met at least 2 out of 3 criteria for the diagnosis of HF (i.e. clinical symptoms and signs of HF, natriuretic peptide elevation, or echocardiographic evidence of left ventricular systolic or diastolic dysfunction) as defined by the European Society of Cardiology.[18] These criteria were similar to those used in the Trivandrum Heart Failure Registry, the first HF registry in Kerala.[5,7,19]

Intervention

We used formative, mixed-methods research to contextualize previously tested components of a quality improvement toolkit to target process of care measures and clinical outcomes in patients hospitalized with acute HF through previously identified gaps in HF care in Kerala[5,7,19], a systematic review[13] key informant interviews[16], and prior acute cardiovascular quality improvement trial experience.[15] The HF QUIK toolkit included an in-hospital and discharge checklist to prompt physicians and nurses to order guideline-recommended in-hospital diagnostics (i.e. electrocardiogram, natriuretic peptide, transthoracic echocardiogram), guideline-directed medical therapy, patient education for HF-specific health behaviors, and follow-up recommendations (e.g. referral for implantable cardioverter defibrillator or cardiac resynchronization therapy in eligible patients, referral for outpatient cardiac rehabilitation, scheduled outpatient clinic follow-up). Sites received personalized audit-and-feedback reports, which included site-specific performance measures guided by established HF quality metrics (Online Supplement).[6] Based on prior research in Kerala demonstrating limited goal-setting among hospital administrators, each hospital site investigator set a HF quality metric to improve based on their personalized audit-and-feedback report.[20] Lastly, the HF QUIK toolkit included patient education materials on lifestyle, diet, and smoking cessation written in the local language of Malayalam.

The study team performed on-site training of the HF QUIK toolkit at each hospital site with the hospital investigator, site study coordinator, and other members of the local quality improvement team. Each 2-hour session included training of cardiac care unit and general cardiology ward nurses on guideline-directed medical therapy for patients with HF and HF QUIK toolkit use. The pre-intervention control period consisted of usual care according to local hospital practice.

Outcomes

The primary outcome was the prescription of guideline-directed medical therapy for patients with HFrEF at discharge including: angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB), beta-blocker, and aldosterone antagonist measured separately and as a combined outcome. Secondary outcomes included rates of: in-hospital electrocardiogram, in-hospital echocardiogram, discharge tobacco and alcohol cessation

counseling in eligible participants, diet counseling, weight monitoring instructions at discharge, referral for outpatient cardiac rehabilitation, referral for implantable cardioverter defibrillator or cardiac resynchronization therapy, outpatient follow-up appointment scheduled at discharge, hospital length of stay, and inpatient mortality.

Statistical analysis

We initiated this study with a calculated total sample size of 156 participants, which would provide 90% power with a two-sided significance level of 0.05 to detect a 24% relative improvement in the primary outcome by the intervention from the anticipated 17% baseline rate of guideline-directed medical therapy (i.e. ACE-I or ARB, beta blocker, and aldosterone antagonist) among patients with HFrEF without contraindications to these medications. This baseline proportion was estimated from the Trivandrum Heart Failure Registry.[5] Date of admission was used to allocate participants to pre-intervention, control period or the intervention period in the analysis. Baseline characteristics are summarized for control and intervention periods. Continuous variables are reported as means with standard deviations or medians with interquartile range if data were skewed, and categorical variables as counts with percentages. We performed multivariable logistic regression analysis to evaluate the odds of adherence to in-hospital process of care measures pre- and post-intervention and quantile regression for the hospital length of stay outcome. The unadjusted model included group variable only (control and intervention period), and the second model was adjusted for age and gender. In the primary analysis, the mixed effect logistic regression model was used adjusting for age, gender, and random effect for hospital. The final model was further adjusted for covariates that are predictors of mortality in the HF risk score developed by the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC).[21] We used interrupted time series models to compare the slopes of monthly control and intervention rates for GDMT, ACE-I or ARB, beta blocker and aldosterone antagonist.[22] We performed a complete case analysis due to low rate of missing data (0.1%). For statistical analyses, Stata, version 14 (Stata Corp), SAS, version 9.4 (SAS Institute Inc), and R, version 3.5.1 (R Foundation), were used.

Results

We recruited 1,469 participants from 8 hospitals in Kerala, India. The hospitals varied in type, including government, non-profit, and private hospitals (Online Table 1). Participants were excluded if there were duplicate data entries for the same participant (n = 13), had missing data (n = 2), or were admitted to the hospital after the final date of study enrollment (n = 54). The complete case analysis was performed on 1,400 participants with 758 participants in the control period and 642 participants in the intervention period (Online Figure 1).

Table 1 describes the baseline characteristics of study participants by control and intervention period. Mean (SD) age of participants was 66.6 (12.2) years, 62% were men, and 36% had a history of tobacco use. More than half of participants had diabetes mellitus (55%), hypertension (58%) and coronary heart disease (56%). The primary etiology of HF was ischemic heart disease (n = 1,204, 86%). Prior to hospital admission, 24% of

participants were prescribed ACE-I or ARB, 34% were prescribed beta-blocker, and 16% were prescribed an aldosterone antagonist. Mean (SD) left ventricular ejection fraction was 35.9% (10.1%) in the control period and 35.1% (9.9%) in the intervention period (p = 0.12).

Table 2 describes in-hospital evaluation and management by control and intervention period. An electrocardiogram was performed during the hospitalization on almost all participants. Less than one quarter (21%) of participants underwent coronary angiography during the hospitalization, and 6% received percutaneous coronary intervention. Approximately 18% of participants were treated with an inotrope during the hospitalization. Although non-invasive positive pressure ventilation was utilized in the care of 28% of participants, use of invasive support devices, such as intra-aortic balloon pump and dialysis or ultrafiltration, was rare.

Table 3 describes crude differences in outcomes between participants in the control and intervention periods, and Table 4 describes the unadjusted and adjusted analyses. The primary outcome of prescription of guideline-directed medical therapy at discharge for participants with HFrEF was achieved in 167 (41.3%) participants in the intervention period compared to 124 (28.2%) participants in the control period (difference 13.2%; 95% CI 6.8, 19.5). The intervention led to 70% higher odds of guideline-directed medical therapy at discharge (adjusted OR 1.70, 95% CI 1.17, 2.46). The highest rate of guideline-directed medical therapy at discharge was observed in the initial weeks following intervention delivery with an insignificant concomitant decline over time (Figure 1, Online Table 2, Online Table 3). There was a 4.9% (95% CI 2.2, 7.5) higher rate in the prescription of diuretics at discharge in participants in the intervention period compared with the control period (adjusted OR 3.15; 95% CI 1.33, 7.46). Discharge process of care measures were higher in participants in the intervention period compared to control period including diet counseling (adjusted OR 2.37; 95% CI 1.38, 4.08), weight monitoring instructions (adjusted OR 2.52; 95% CI 1.49, 4.28) and scheduling of outpatient clinic follow-up appointment (adjusted OR 3.81; 95% CI 2.27, 6.39). There was a 3% (95 CI −5.9, −0.1) lower rate of referral for implantable cardioverter defibrillator among participants in the intervention period compared with the control period. There was no difference in hospital length of stay (adjusted beta coefficient 0.0; 95% CI −0.92, 0.92) nor inpatient mortality (adjusted OR 1.04, 95% CI 0.70, 1.54) between participants enrolled during both control and intervention periods.

Discussion

Among 1,400 participants admitted with acute HF in Kerala, a locally-contextualized quality improvement toolkit significantly increased the prescription of guideline-directed medical therapy with 70% higher odds at hospital discharge among participants in the intervention period compared to the control period. The intervention also increased the rates of discharge process of care measures including tobacco cessation counseling, alcohol cessation counseling, diet counseling, weight monitoring instructions, and scheduling of outpatient clinic follow-up appointments. There was no effect on hospital length of stay nor inpatient mortality. To our knowledge, this is the first quasi-experimental study evaluating the effect of an in-hospital quality improvement intervention for patients with acute HF in a low-or middle-income country.[13]

Guideline-directed medical therapy substantially reduces morbidity and mortality of patients with HFrEF and is considered among the highest priority interventions for inclusion in universal health coverage packages.[1] Among patients with HFrEF, the relative risk reduction in mortality for ACE-I or ARB is 17% (number needed to treat [NNT] standardized to 36 months for mortality reduction = 26), beta blocker is 34% (NNT = 9), and aldosterone receptor antagonist is 30% (NNT = 6).[23] There is increased clinical effectiveness and incremental reduction in risk of death when these pharmacotherapies are used in combination.[24] Survival benefits from these medications can translate to large gains in clinical outcomes of HF patients by increasing prescription of guideline-directed medical therapy, which remain low in low- and middle-income countries. For example, a 2014 systematic review of HF care in low-and middle-income countries including 53 studies of 237,908 patients revealed suboptimal treatment rates with ACE-I (57%; 95% CI 49%, 64%), beta-blockers (34%; 95% CI 28%, 41%), and aldosterone receptor antagonists (32%; 95% CI 25%, 39%).[4] The Trivandrum Heart Failure Registry demonstrated even lower rates of optimal treatment with combined guideline-directed medical therapy at discharge in only 25% of patients with HFrEF.[5] Low prescription rates of ACE-I or ARB, beta-blocker, and aldosterone receptor antagonist prior to admission in our study highlight the opportunity to increase guideline-directed medical therapy during hospitalization in India, particularly as pre-discharge initiation improves future adherence.[25]

Randomized trials have not demonstrated a consistent effect of in-hospital quality improvement interventions on process of care measures or clinical outcomes for patients with acute HF.[13] The largest trial to date (147 hospitals, 71,829 participants in the Get With The Guidelines-Heart Failure [GWTG-HF] quality improvement program) demonstrated no improvement in prescription of guideline-directed medical therapy at discharge.[6] In comparison to the GWTG-HF trial in the United States, baseline quality of care was lower in the current study, which might partially explain the observed differences between these two studies.

The Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study assessed whether public release of hospital-specific quality indicators could improve quality of care of patients hospitalized with acute myocardial infarction or HF in 86 hospitals (n = 17,544 participants) in Canada.[26] Although the investigators found no improvement in their primary outcome of a composite HF process-of-care metric, there was 5.9% (95% CI 1.0%, 10.7%) increase in ACE-I or ARB prescription for patients with left ventricular dysfunction in the intervention group. Our intervention demonstrated a similar increase in prescription of ACE-I or ARB, as well as higher rates of beta-blocker and aldosterone receptor antagonist at discharge. The larger effect of the current study's intervention on process of care measures compared with the EFFECT study may be due to lower baseline medication rates, greater acceptability among providers and health systems, higher adoption and fidelity of the intervention, and more actionable information presented in the hospital-specific audit-and-feedback reports.

Prior mixed methods research in Kerala suggests low levels of targetable goal-setting behavior amongst hospital managers is associated with worse cardiovascular health outcomes in the region.[20] By incorporating these data into the development of our intervention and enabling each hospital investigator to target one process of care measure to

improve at their site based on the personalized audit-and-feedback report, the feedback-action loop may have been tightened. Whether gains in process of care measures at discharge translate to improvements in long-term clinical outcomes remains uncertain and warrants further investigation.[15]

This study has several strengths. First, to our knowledge, this is the first quasi-experimental study evaluating the effect of an in-hospital, quality improvement intervention for patients with acute HF in India, or any a low- or middle-income country.[13] Second, we used formative, mixed-methods research to contextualize previously tested components of a quality improvement toolkit through previously identified gaps in HF care in Kerala [5,7,19], a systematic review [13] and key informant interviews.[16] Third, our collaboration with local and national stakeholders, including prior cardiovascular quality improvement trial experience[15], supported the implementation of this study. Fourth, we utilized a rigorous interrupted time series study design in an unselected population leading to greater external validity.[27,28]

This study has several limitations. First, it is unknown which components of the complex intervention led to improvements in process of care measures. Second, the short duration of the study limited evaluation of the sustained effect of the intervention. Third, this study is susceptible to selection bias due to lack of randomization, even though interrupted time series design is considered a rigorous quasi-experimental study design.[27,28] Fourth, baseline temporal trends in guideline directed medical therapy over the study period suggest that the observed results may be partially driven by the Hawthorne effect wherein the process of observation changes the measure that is being observed.

Conclusion

This quasi-experimental study in Kerala demonstrated improvements in guideline-directed medical therapy at hospital discharge using a HF-specific quality improvement toolkit. Implementation of this intervention may improve HF care in other settings in India and other low- or middle-income countries.[13] Although significant gains in process of care measures were demonstrated in this study, further investigation is needed to continue to improve clinical outcomes for patients with HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

HF	heart failure
HFrEF	heart failure with reduced ejection fraction

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Highlights

- Although quality improvement interventions for acute heart failure have been studied in high-income countries without a consistent effect on process of care measures and clinical outcomes, none have been studied in low- or middle-income country settings where quality of care can be lower.
- To our knowledge, this is the first quasi-experimental study evaluating the effect of an in-hospital quality improvement intervention for patients with acute heart failure in a low-or middle-income country. Findings from this study support implementation of locally-contextualized quality improvement toolkits to increase rates of guideline-directed medical therapy for patients with acute heart failure at hospital discharge.
- Broader implementation of this quality improvement intervention may improve heart failure care in low- and middle-income countries.

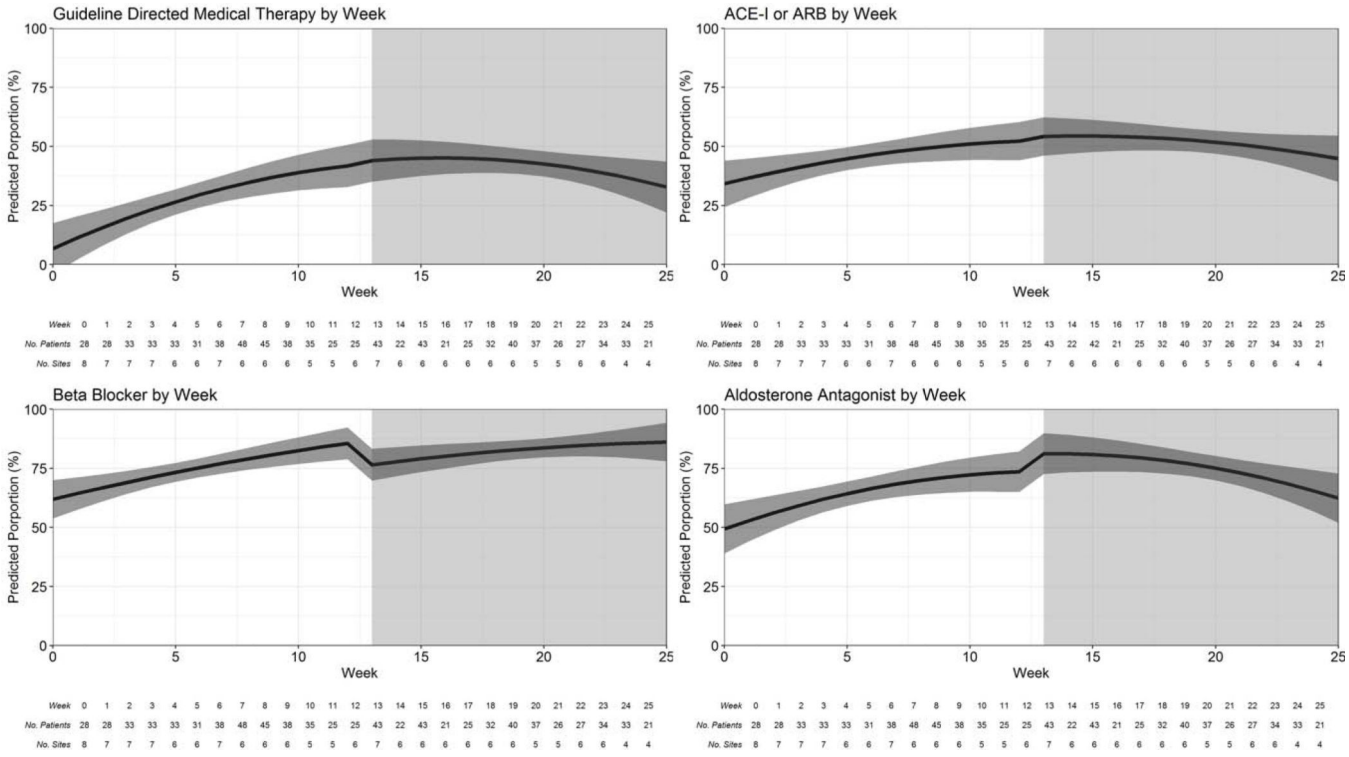

Figure 1.

Rate of guideline-directed medical therapy over time in HF QUIK. **Figure Legend:** Interrupted time series model graphs for the primary outcome of guideline-directed medical therapy (A); its components: ACE-I or ARB (B), beta-blocker (C) and aldosterone antagonist (D) are shown. The white background indicates control period and grey background indicates intervention period.

ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker.

Table 1.

Baseline characteristics of HF QUIK participants by control and intervention period.

	Control		Intervention		P-value
Participant characteristics	**N**	**n (%)**	**N**	**n (%)**	
Age, mean (SD), y	758	66.7 (12.4)	642	66.5 (12.0)	0.78
Male	758	441 (58.2)	642	423 (65.9)	0.003
Transferred from another facility	758	282 (37.2)	642	225 (35.0)	0.57
Ischemic etiology of HF	757	634 (83.8)	642	570 (88.8)	<0.001
Medical history prior to HF admission					
Tobacco use,	756	267 (35.3)	642	233 (36.3)	0.21
Alcohol use	756	187 (24.7)	642	154 (24.0)	0.24
Coronary heart disease	758	409 (54.0)	642	377 (58.7)	0.07
Percutaneous coronary intervention	758	67 (8.8)	642	62 (9.7)	0.60
Diabetes mellitus	758	428 (56.5)	642	339 (52.8)	0.17
Hypertension	758	447 (59.0)	642	371 (57.8)	0.66
Hyperlipidemia	758	161 (21.2)	642	134 (20.9)	0.87
Valvular heart disease	758	52 (6.9)	642	36 (5.6)	0.34
Rheumatic heart disease,	758	24 (3.2)	642	21 (3.3)	0.91
Chronic kidney disease	758	129 (17.0)	642	97 (15.1)	0.33
Stroke	758	54 (7.1)	642	42 (6.5)	0.67
Implantable cardioverter defibrillator	758	5 (0.7)	642	4 (0.6)	0.93
Cardiac resynchronization therapy	758	5 (0.7)	642	4 (0.6)	0.93
Medications prior to HF admission					
Loop diuretic	758	297 (39.2)	642	258 (40.2)	0.70
Thiazide diuretic	758	8 (1.1)	642	8 (1.2)	0.74
ACE-I or ARB	758	179 (23.6)	642	156 (24.3)	0.77
Beta-blocker	758	233 (30.7)	642	247 (38.5)	0.002
Aldosterone antagonist	758	135 (17.8)	642	87 (13.6)	0.03
ARNi	758	10 (1.3)	642	3 (0.5)	0.10
Digoxin	758	78 (10.3)	642	52 (8.1)	0.16
Ivabradine	758	34 (4.5)	642	20 (3.1)	0.19
Aspirin	758	334 (44.1)	642	318 (49.5)	0.04
Statin	758	347 (45.8)	642	330 (51.4)	0.04
Physical exam, laboratory and imaging					
Weight, mean (SD), kg	400	63.6 (11.4)	399	64.2 (10.6)	0.45
Systolic blood pressure, mean (SD), mmHg	755	138.7 (30.1)	639	141.4 (30.5)	0.10
Diastolic blood pressure, mean (SD), mmHg	755	82.4 (15.5)	639	83.5 (15.5)	0.18
Heart rate, mean (SD), bpm	757	93.5 (23.3)	640	94.1 (23.8)	0.65
Sodium, mean (SD), mEq/L	746	134.6 (6.3)	638	134.8 (5.1)	0.68
Creatinine, median (IQR), mg/dL	749	1.2 (1.0, 1.6)	638	1.2 (1.0, 1.7)	0.87
BNP, median (IQR), pg/dL	72	2,665 (1,295, 7,398)	84	2,331 (1,441, 8,780)	0.66

	Control		Intervention		P-value
Participant characteristics	**N**	**n (%)**	**N**	**n (%)**	
NT pro-BNP, median (IQR), pg/mL	53	4,322 (2,215, 12,071)	39	6,487 (2,957, 12,260)	0.23
Ejection fraction, mean (SD), %	752	35.9 (10.1)	638	35.1 (9.9)	0.12

ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, ARNi: angiotensin receptor neprilysin inhibitor, BNP: B-type natriuretic peptide, IQR: interquartile range, NT pro-BNP: N-terminal pro hormone B-type natriuretic peptide

Table 2.

In-hospital tests, procedures, and treatment of HF QUIK participants by control and intervention period.

Diagnostic tests and treatment	Control (n = 758)[1]	Intervention (n = 642)[1]	P-value
In-hospital tests and procedures			
ECG, No. (%)	751 (99.1)	641 (99.8)	0.06
Cardioversion, No. (%)	23 (3.0)	14 (2.2)	0.32
Stress testing, No. (%)	1 (0.1)	0 (0.0)	0.36
Coronary angiography, No. (%)	163 (21.5)	133 (20.7)	0.72
Percutaneous coronary intervention, No. (%)	45 (5.9)	44 (6.9)	0.48
Coronary artery bypass graft, No. (%)	6 (0.8)	9 (1.4)	0.27
Implantable cardioverter defibrillator, No. (%)	4 (0.5)	3 (0.5)	0.87
Cardiac resynchronization therapy, No. (%)	1 (0.1)	3 (0.5)	0.24
Intra-aortic balloon pump, No. (%)	0 (0.0)	1 (0.2)	0.28
Dialysis or ultrafiltration, No. (%)	8 (1.1)	9 (1.4)	0.56
Non-invasive positive pressure ventilation, No. (%)	218 (28.8)	173 (26.9)	0.45
Mechanical ventilation, No. (%)	68 (9.0)	57 (8.9)	0.95
In-hospital treatment			
Loop diuretic, No. (%)	713 (94.1)	631 (98.3)	<0.001
Thiazide diuretic, No. (%)	16 (2.1)	16 (2.5)	0.63
ACE-I or ARB, No. (%)	310 (40.9)	283 (44.1)	0.23
Beta-blocker, No. (%)	542 (71.5)	478 (74.5)	0.22
Aldosterone antagonist, No. (%)	436 (57.5)	431 (67.1)	<0.001
ARNi, No. (%)	17 (2.2)	8 (1.2)	0.16
Digoxin No. (%)	153 (20.2)	107 (16.7)	0.09
Ivabradine, No. (%)	78 (10.3)	70 (10.9)	0.71
Aspirin, No. (%)	632 (83.4)	556 (86.6)	0.09
Statin, No. (%)	638 (84.2)	559 (87.1)	0.12
Hydralazine-nitrate, No. (%)	45 (5.9)	23 (3.6)	0.04
Nitroglycerin, No. (%)	219 (28.9)	204 (31.8)	0.24
Inotrope, No. (%)	129 (17.0)	126 (19.6)	0.21

ECG: electrocardiogram, ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, ARNi: angiotensin receptor neprilysin inhibitor

[1]Data were completely reported for all variables in Table 2.

Table 3.

Process of care measures and clinical outcomes of HF QUIK participants by control and intervention period.

	Control (n=758)		Intervention (n=642)		Difference (95% CI)[1]
	N	n (%)	N	n (%)	
Discharge process of care measures[2]					
GDMT at discharge[3]	440	124 (28.2)	404	167 (41.3)	13.2 (6.8, 19.5)
ACE-I or ARB at discharge[3]	440	200 (45.5)	403	207 (51.4)	5.9 (−0.8, 12.7)
Beta-blocker at discharge[3]	440	333 (75.7)	404	332 (82.2)	6.5 (1.0, 12.0)
Aldosterone antagonist at discharge[3]	440	286 (65.0)	404	305 (75.5)	10.5 (4.4, 16.6)
Diuretic at discharge[3]	440	411 (93.4)	404	397 (98.3)	4.9 (2.2, 7.5)
Tobacco cessation counseling[4]	420	266 (63.3)	355	229 (64.5)	1.2 (−5.6, 8.0)
Alcohol cessation counseling[4]	407	246 (60.4)	343	213 (62.1)	1.7 (−5.3, 8.7)
Diet counseling	689	589 (85.5)	587	510 (86.9)	1.4 (−2.4, 5.2)
Weight monitoring instructions	689	576 (83.6)	587	507 (86.4)	2.8 (−1.2, 6.7)
Referral to outpatient cardiac rehabilitation	690	30 (4.3)	586	16 (2.7)	−1.6 (−3.6, 0.4)
Referral for ICD therapy[5]	364	20 (5.5)	322	8 (2.5)	−3.0 (−5.9, −0.1)
Outpatient clinic follow-up scheduled	690	618 (89.6)	587	565 (96.3)	6.7 (3.9, 9.4)
In-hospital process of care measures					
ECG	758	751 (99.1)	642	641 (99.8)	0.8 (0.02, 1.5)
Transthoracic echocardiogram	757	710 (93.8)	642	591 (92.1)	−1.7 (−4.4, 1.0)
Clinical outcomes					
Hospital length of stay, median (IQR), days	756	4 (3–6)	641	4 (3–6)	0.0 (−0.3, 0.3)
Inpatient mortality	756	66 (8.7)	642	55 (8.6)	−0.2 (−3.1, 2.8)

[1] Crude difference: Intervention minus control calculated either as a risk difference percentage for count data or difference in medians for continuous nonparametric data.

[2] Among participants discharged; N = 1279 with 692 in control period and 587 in intervention period

[3] Among participants discharged with LVEF <40%; N = 846 with 442 in control period and 404 in intervention period

[4] Among participants who reported tobacco or alcohol use; N = 775 and N = 750 for tobacco and alcohol use respectively

[5] Among participants with LVEF ≤35%; N = 688 with 366 in control period and 322 in intervention period

ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, GDMT: guideline-directed medical therapy, ICD: implantable cardioverter defibrillator, LVEF: center ventricular ejection fraction, ECG: electrocardiogram

Table 4.

Unadjusted and adjusted odds of process of care measures and clinical outcomes in HF QUIK.

	N	OR (95% CI)			
		Unadjusted	Age and sex adjusted	Primary analysis[1]	MAGGIC adjusted analysis[2]
Discharge process of care measures[3]					
GDMT at discharge[4]	844	1.80 (1.35, 2.39)	1.82 (1.37, 2.43)	1.70 (1.17, 2.46)	1.81 (1.21, 2.70)
ACE-I or ARB at discharge[4]	843	1.27 (0.97, 1.66)	1.30 (0.99, 1.71)	1.00 (0.72, 1.39)	0.94 (0.66, 1.34)
Beta-blocker at discharge[4]	844	1.48 (1.06, 2.07)	1.48 (1.06, 2.07)	2.15 (1.38, 3.35)	2.26 (1.44, 3.56)
Aldosterone antagonist at discharge[4]	844	1.66 (1.23, 2.24)	1.67 (1.24, 2.26)	2.16 (1.47, 3.17)	2.26 (1.51, 3.37)
Diuretic at discharge[4]	844	4.00 (1.73, 9.24)	4.02 (1.74, 9.30)	3.15 (1.33, 7.46)	2.98 (1.25, 7.11)
Tobacco cessation counseling[5]	775	1.05 (0.78, 1.41)	0.87 (0.61, 1.25)	1.50 (0.91, 2.48)	1.44 (0.86, 2.40)
Alcohol cessation counseling[5]	750	1.07 (0.80, 1.44)	0.93 (0.66, 1.32)	1.64 (0.99, 2.72)	1.67 (0.99, 2.82)
Diet counseling	1276	1.12 (0.82, 1.55)	1.11 (0.81, 1.54)	2.37 (1.38, 4.08)	2.29 (1.33, 3.95)
Weight monitoring instructions	1276	1.24 (0.91, 1.70)	1.23 (0.90, 1.68)	2.52 (1.49, 4.28)	2.45 (1.44, 4.16)
Referral to outpatient cardiac rehabilitation	1276	0.62 (0.33, 1.14)	0.62 (0.33, 1.15)	0.60 (0.32, 1.13)	0.57 (0.30, 1.08)
Referral for ICD therapy[6]	686	0.44 (0.19, 1.01)	0.44 (0.19, 1.01)	0.39 (0.16, 0.94)	0.39 (0.16, 0.94)
Outpatient clinic follow-up scheduled	1277	2.99 (1.83, 4.89)	3.02 (1.84, 4.93)	3.81 (2.27, 6.39)	3.88 (2.29, 6.57)
In-hospital process of care measures					
ECG	1400	5.97 (0.73, 48.69)	6.03 (0.74, 49.30)	5.21 (0.62, 43.80)	4.66 (0.54, 40.06)
Transthoracic echocardiogram	1399	0.77 (0.51, 1.16)	0.75 (0.50, 1.14)	0.90 (0.55, 1.46)	0.89 (0.53, 1.48)
Clinical outcomes					
Hospital length of stay[7]	1397	0.0 (−0.50, 0.50)	0.0 (−0.50, 0.50)	0.0 (−0.92, 0.92)	0.0 (−0.48, 0.48)
Inpatient mortality	1398	0.98 (0.67, 1.42)	0.98 (0.67, 1.42)	1.04 (0.70, 1.54)	1.03 (0.69, 1.55)

[1] Adjusted for age, sex and random cluster effect for hospital.

[2] Adjusted for age, sex, random cluster effect for hospital, and measured MAGGIC risk predictors including ejection fraction, serum creatinine, and diabetes mellitus.

[3] Among participants discharged; N = 1279 with 692 in control period and 587 in intervention period.

[4]Among participants discharged with LVEF <40%; N = 846 with 442 in control period and 404 in intervention period.

[5]Among participants who reported tobacco or alcohol use; N = 775 and N = 750 for tobacco and alcohol use respectively.

[6]Among participants with LVEF ≤35%; N = 688 with 366 in control period and 322 in intervention period.

[7]Effect estimates are Beta coefficients from quantile regression models.

GDMT: guideline-directed medical therapy, ACE-I: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, ICD: implantable cardioverter defibrillator, LVEF: left ventricular ejection fraction, ECG: electrocardiogram, MAGGIC: Meta-Analysis Global Group in Chronic Heart Failure