

# Heart Failure Patients Receiving ACEIs/ARBs were Less Likely to be Hospitalized or to Use Emergency Care in the Following Year

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## Background

Heart failure (HF) is a severe chronic illness with high attributable morbidity, mortality, and cost (Jessup et al., 2009). In multiple randomized-controlled trials, angiotensin-converting enzyme inhibitors (ACEIs) have been shown to decrease HF morbidity and mortality (The CONSENSUS Trial Study Group, 1987; Flather et al., 2000; The SOLVD Investigators, 1991, 1992), and angiotensin receptor blockers (ARBs) have been beneficial for those who cannot tolerate ACEI therapy (Granger et al., 2003; Jong, Demers, McKelvie, & Liu, 2002; Pfeffer et al., 2003; Pitt et al., 2000; Ram, 2008). There are many observational studies verifying the clinical benefits of ACEIs among patients discharged with HF, but they have not looked at a broad inventory of utilization measures (e.g., emergency department visits), have not included ARBs, or have mainly focused on a particularly sick population (hospital discharges), rather than a broad cross section of individuals in care (Ahmed, Centor, Weaver, & Perry, 2005; Ahmed, Kiefe, Allman, Sims, & DeLong, 2002; Ahmed, Maisiak, Allman, DeLong, & Farmer, 2003; Gotsman, Rubonivich & Azaz-Livshits, 2008; Grigorian Shamagian et al., 2006; Hess, Preblich, Hill, Plauschinat, & Yaskin, 2009; Johnson, Jin, Quan & Cujec, 2003; Keyhan, Chen, & Pilote, 2007; Pedone, Pahor, Carosella, Bernabei, & Carbonin, 2004; Rochon et al., 2004; Tribouilloy et al., 2008). Indeed, data supporting the benefit of ACEIs or ARBs on the utilization patterns of HF patients in “real-world” settings are comparatively sparse, even though comparing cardiovascular care is one of the highest-priority areas for comparative effectiveness research identified by the Institute of Medicine (Initial National Priorities for Comparative Effectiveness Research, 2009). In particular, it is unclear whether the receipt of ACEIs/ARBs reduces hospitalizations and emergency room (ER) visits.

Investigating the benefit of ACEIs/ARBs among HF patients seen in both inpatient

**Abstract:** Angiotensin-converting enzyme inhibitors (ACEIs) have been shown to decrease morbidity and mortality in heart failure (HF) patients in randomized-controlled trials; observational studies have confirmed this benefit among patients discharged with HF. Investigating the benefit of ACEIs or angiotensin receptor blockers (ARBs) among general HF patients has important implications for quality-of-care measurement and quality initiatives. The objective of this study is to assess the impact of receipt of ACEIs/ARBs among patients with HF on hospitalization, emergency care, and healthcare cost during the following year. Using administrative data, we identified HF patients between 2000 and 2005 in a large health plan ( $n = 2,396$  patients). We conducted multivariate analysis to assess the impact of receipt of an ACEI/ARB on likelihood of hospitalization and emergency care, and on total healthcare cost. We found that patients who received ACEIs/ARBs were less likely to be hospitalized (odds ratio [OR] = 0.82,  $p < .05$ ) or use emergency care (OR = 0.82,  $p < .05$ ) in the following year. Receipt of ACEIs/ARBs was not associated with significantly increased cost. Incentivizing the receipt of ACEIs/ARBs in a general population with HF may be a suitable target for pay-for-performance programs, disease management programs, or newer complementary frameworks, such as value-based insurance design.

and outpatient settings has important implications for quality-of-care measurement and development of incentive programs, such as pay-for-performance (P4P). Because multiple studies have demonstrated that ACEIs/ARBs are underutilized among patients with HF (Bart et al., 1999; Echemann et al., 2000; Edep, Shah, Tateo, & Massie, 1997; Kermani, Dua, & Gradman, 2000; McDermott et al., 1997; Smith et al., 1998; Stafford & Radley, 2003), many different programs have already been adopted by payers to incentivize the prescription of ACEIs/ARBs (e.g., P4P), even though little data support the benefit of the incentivized behavior (ACEI/ARB) in those settings. To infer whether these programs should be expanded or redirected, it is important to ask whether the receipt of ACEIs/ARBs is associated with improved outcomes and utilization measures in “real-world” settings.

## Keywords

ACEI/ARB  
acute utilization  
congestive heart failure  
cost

The objective of this study was to assess the impact of filling  $\geq 1$  prescription of an ACEI/ARB among patients identified with HF on utilization measures that correlate with poor clinical outcomes (hospitalizations and emergency care), using an administrative claims algorithm. Because healthcare costs are increasingly important, we also investigated the impact of ACEI/ARB prescriptions on overall healthcare costs.

## Methods

### *Data and Sample*

We used deidentified administrative claims data from a large health plan in Hawaii. This health plan had implemented a physician P4P program that not only incentivized physicians to write at least one prescription for an ACEI/ARB, but also included a concurrent disease management program for HF patients during this time frame (Chung, Chernicoff, Nakao, Nickel, & Legorreta, 2003). Patients  $\geq 18$  years of age with at least one inpatient HF encounter (ICD-9 diagnosis code(s): 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 428.0, 428.1, 428.20–428.23, 428.40–428.43), two outpatient HF encounters and HF medication (e.g., digoxin, diuretics, etc.), or three HF outpatient encounters within a 1-year period between 2000 and 2005 were identified and followed for at least 1 year (through 2006). Using this algorithm, only 17% of the patients were identified via an inpatient claim. The majority of the HF patients were identified via outpatient encounters. To ensure that we had complete data, we included only patients who were continuously enrolled in medical and pharmacy benefits for at least 2 years. We excluded patients with a contraindication for an ACEI/ARB (i.e., hypotension, hyperkalemia, angioedema, acute renal failure, or those on dialysis). The final sample was comprised of 2,396 patients and encompassed 3,767 patient-years.

### *Dependent Variables*

The outcomes measured included hospitalizations, ER use, and total healthcare cost (USD). To calculate cost, we used the maximum amount the health plan would pay for a specific claim (“allowed” amount) and the gross domestic product (GDP) index adjusted to 2006 USD.

### *Main Independent Variables and Covariates*

The main independent variable was the incentivized quality care process of the P4P program, the filling of at least one ACEI/ARB prescription within a 1-year period. Covariates included age ( $<50$ , 50–65,  $\geq 65$  years), gender, comorbidity score, medication burden, having seen a cardiologist, baseline acute utilizations, baseline cost, and calendar year. Comorbidity was measured using the Elixhauser comorbidity score, which was calculated using diagnosis codes (Elixhauser, Steiner, Harris, & Coffey, 1998; Healthcare Cost and Utilization Project [HCUP]). HF was excluded as a comorbidity in this cohort. Medication burden was the number of distinct medication types that patients had filled within a 1-year period, excluding ACEIs/ARBs. Based on the distribution of the medication burden, this variable was dichotomized to  $\geq 10$  medication types (y/n). All outcomes were measured during the year after the covariates/independent variable were defined because the goal was to assess the impact of the covariates/independent variable (i.e., age, gender, receipt of quality care) on outcomes (i.e., hospitalization) and not outcomes on the covariates/independent variable.

### *Statistical Analyses*

Because a single patient generally had multiple years of follow-up, we used patient-year as the unit of analysis. Hierarchical logistic regressions accounting for the nesting of years within patients were utilized to assess the impact of ACEIs/ARBs on hospitalization in the following year while controlling for age, gender, prior hospitalization, medication burden, having seen a cardiologist, comorbidity score, and calendar year. A second hierarchical logistic regression model accounting for the nesting of years within patients was used to assess the impact of ACEIs/ARBs on ER use in the following year, while controlling for age, gender, prior ER use, medication burden, having seen a cardiologist, comorbidity score, and calendar year. Lastly, to assess the impact of ACEIs/ARBs on total healthcare costs in the following year, we used a hierarchical log-transformed linear model accounting for the nesting of years within patients, while controlling for age, gender, medication burden, having seen a cardiologist, comorbidity score, prior healthcare cost, and year. Our hierarchical models

did not cluster by hospitals because only 17% were treated by a hospital at baseline. Additionally, we did not cluster by physicians because, on average, many physicians were involved in the care of each patient.

Variables were assessed for collinearity before their inclusion in the multivariate models. The results of the logistic regressions were presented as odds ratios (ORs) with 95% confidence intervals (CIs); the results of the log-transformed linear model were presented as coefficient estimates with 95% CIs. We calculated the adjusted percent of hospitalization and ER use for patients who had filled and had not filled at least one prescription of an ACEI/ARB separately using the multivariate model estimates. SAS<sup>®</sup> Proprietary Software, Release 9.1 (SAS Institute Inc., Cary, NC) was used for all statistical analyses. A *p* value <.05 was considered to be significant. This study was determined to be research without “human subjects” involvement by an independent IRB.

## Results

The majority of HF patients were  $\geq 65$  years of age and male (Table 1). Across all years, over 70% of patients received an ACEI/ARB. Among patients who received at least one prescription of ACEI/ARB, 80% had received five or more scripts. Both comorbidity scores and medication burdens remained stable over the years of the study, ranging from 2.4 to 2.6 and 8.9 to 9.8, respectively. Hospitalization rates rose to a high of 20.3% in 2002, and fell to 15.8% by 2006. ER visits reached a high of 28.7% in 2004, but had decreased to 24.8% in 2006. Over the years, total healthcare cost ranged from US\$9,667 to US\$12,920, with inpatient and outpatient costs being the largest components.

Patients who received at least one prescription of an ACEI/ARB were significantly less likely to be hospitalized (adjusted percent 26% vs. 30%, OR = 0.82, 95% CI: 0.68–0.99, *p* < .05) or use the ER (adjusted percent 33% vs. 37%, OR = 0.82, 95% CI: 0.70–0.97, *p* < .05) in the following year (Table 2). Other significant predictors of hospitalization included age  $\geq 65$  years, prior history of hospitalization, filling  $\geq 10$  prescription drug types, and greater comorbidity score. Similarly, significant predictors of ER use included prior history of ER use, filling  $\geq 10$  prescription drug types, and

greater comorbidity score. Gender was not a significant predictor of either hospitalization or ER use.

Receipt of an ACEI/ARB was not significantly associated with increased total healthcare cost. However, older patients, patients with greater medication burden, patients with more comorbid conditions, and patients with higher baseline healthcare costs were associated with significantly higher healthcare costs in the following year. There was no significant difference in total healthcare cost associated with gender, having seen a cardiologist, or calendar year (Table 3).

## Discussion

Our results suggested that HF patients in a “real-world” setting who filled at least one prescription of an ACEI/ARB had decreased acute care utilization during the following year. Specifically, this study showed a 13% decrease in the likelihood of hospitalization, and a 19% decrease in the likelihood of emergency care. In addition, when adjusted for factors such as comorbidity, our results suggested that receipt of an ACEI/ARB was not associated with significantly increased total healthcare cost, because the increase in pharmacy expenditures was offset by savings from less inpatient and ER utilization. Additionally, although our algorithm was consistent with the P4P quality measure requiring only one ACEI/ARB prescription, the majority of patients filled five or more prescriptions; these scripts were all included in the cost calculation and did not lead to an increase in healthcare expenditures. This finding is consistent with prior publications, describing interventions such as providing comprehensive diabetes care and colon cancer screening, which have been shown to be cost effective (Eastman et al., 1997; Maciosek, Solberg, Coffield, Edwards, & Goodman, 2006). We found that older patients, patients who were hospitalized in the year prior, patients with high medication burden, and patients with greater comorbidity were more likely to be hospitalized, raising the possibility that the absolute impact of ACEI/ARB prescriptions on utilization may be larger in these groups.

Our results showed a 13% decrease in hospitalization rates in the ACEI/ARB group, whereas large randomized trials have shown decreases of greater magnitude (22–26%; The SOLVD Investigators, 1991; Pfeffer et al.,

**Table 1. Characteristics of Heart Failure Patients by Year**

	2000 (n = 719)	2001 (n = 614)	2002 (n = 636)	2003 (n = 633)	2004 (n = 581)	2005 (n = 584)	2006 (n = 532)
Age <50 (%)	5.6	7.0	7.2	9.3	10.3	10.6	8.5
50 ≤ Age < 65 (%)	23.2	25.4	29.1	29.9	31.2	31.3	29.9
Age ≥ 65 (%)	71.2	67.6	63.7	60.8	58.5	58.1	61.7
Female (%)	38.5	39.6	38.2	35.7	38.0	38.5	43.1
Elixhauser comorbidity score (mean ± SD)	2.4 ± 1.6	2.4 ± 1.5	2.5 ± 1.5	2.6 ± 1.7	2.6 ± 1.7	2.6 ± 1.5	2.6 ± 1.6
Medication burden <sup>a</sup> (mean ± SD)	9.5 ± 4.8	9.3 ± 4.8	8.9 ± 4.9	9.4 ± 4.9	9.8 ± 4.8	9.4 ± 4.7	9.0 ± 4.5
ACEI/ARB use	71.1	71.8	76.6	73.8	78.1	72.8	72.7
Hospitalization (%)	17.9	18.6	20.3	19.1	18.6	15.8	15.8
ER visit (%)	22.1	26.9	26.3	26.2	28.7	24.7	24.8
Total healthcare cost (mean ± SD; 2006 USD)	9,667 ± 17,008	10,344 ± 17,560	10,667 ± 16,622	12,852 ± 21,080	12,920 ± 18,126	11,978 ± 18,129	10,947 ± 14,525
Outpatient	2,918 ± 3,372	2,959 ± 4,209	4,119 ± 6,893	5,116 ± 12,472	4,786 ± 7,109	4,679 ± 6,531	4,038 ± 5,309
Inpatient	4,309 ± 15,884	4,820 ± 16,058	4,467 ± 13,971	4,669 ± 15,418	4,885 ± 14,590	4,121 ± 15,234	3,948 ± 12,142
Pharmacy	2,440 ± 1,845	2,565 ± 1,965	2,081 ± 1,702	3,067 ± 2,414	3,249 ± 2,783	3,178 ± 2,628	2,960 ± 2,391
Seeing a cardiologist (%)	60.9	58.6	67.3	67.9	70.2	72.8	70.1

Note. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ER = emergency room.

<sup>a</sup>Mean number of unique medications taken by patients during the baseline year, excluding ACEI/ARBs.

**Table 2. Impact of Receipt of an ACEI/ARB on Utilization in the Following Year among Heart Failure Patients**

	Hospitalization (Y/N) OR (95% CI) (n = 2,396)	Emergency Room (Y/N) OR (95% CI) (n = 2,396)
Received ACEI/ARB (reference: no)	0.82 (0.68–0.99)*	0.82 (0.70–0.97)*
Age (reference: <50 years)		
50–64 years	1.07 (0.75–1.52)	0.76 (0.57–1.01)
≥ 65 years	1.74 (1.25–2.43)**	1.26 (0.96–1.66)
Female (reference: male)	0.99 (0.84–1.17)	1.25 (0.96–1.64)
History of hospitalization (reference: no)	1.65 (1.33–2.04)***	—
History of ER utilization (reference: no)	—	2.51 (2.14–2.95)***
≥ 10 drug types (reference: <10 drug types)	1.82 (1.37–2.41)***	1.61 (1.26–2.07)***
Seen by a cardiologist (reference: no)	0.96 (0.81–1.14)	0.96 (0.82–1.11)
Elixhauser comorbidity score	1.15 (1.09–1.21)***	1.06 (1.01–1.11)*
Year (reference: 2005)		
2000	1.26 (0.96–1.65)	1.08 (0.85–1.38)
2001	1.44 (1.10–1.90)**	1.25 (0.97–1.61)
2002	1.25 (0.94–1.64)	1.25 (0.97–1.60)
2003	1.16 (0.88–1.53)	1.16 (0.90–1.49)
2004	1.06 (0.80–1.41)	1.18 (0.91–1.52)

Note. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CI = confidence interval; ER = emergency room; OR = odds ratio.

\*  $p$  value < .05,

\*\*  $p$  value < .01,

\*\*\*  $p$  value < .001.

1992). We hypothesized that our observed decline in hospitalizations was more modest because of a dose-response effect (e.g., our patient population was only required to have filled one prescription, whereas, in these randomized trials, patients were closely monitored to ensure that ACEI/ARB's were being taken consistently); however, true differences in magnitude of ACEI/ARB effect between ideal (e.g., efficacy) and real-world (e.g., effectiveness) settings may also have been an important contributor. That said, a 13% decrease in hospitalization demonstrated a substantial utilization effect from a minimal prescription requirement in a real-world setting. Furthermore, there is the possibility that hospitalization rates could be further decreased through more vigilant medication monitoring by physicians.

A previous study by Abarca, Malone, Armstrong, and Zachry (2004) also sought to identify the impact of ACEI in HF managed care patients using administrative claims data. In addition to finding fewer hospitalizations, they also found that total costs were lower in the ACEI group. However, Abarca and colleagues did not include patients on ARBs in the ACEI group, because ARBs are significantly more expensive than

ACEIs, this grouping may have offset cost reductions elsewhere more completely in our study. Our study is likely generalizable to a wide range of practice settings, in which ARBs may be readily substituted for ACEIs in patients with contraindications to ACEIs.

Our study has notable limitations. First, the selection bias of patients who received ACEIs/ARBs may have accounted for the results presented. However, our data revealed that, at baseline, patients who received ACEIs/ARBs had higher rates of hospitalization per 1,000 than patients who did not receive ACEIs/ARBs (280 vs. 270,  $p < .05$ ). Thus, this selection bias may have led to an underestimation of the benefits of ACEIs/ARBs, rather than an overestimation. Second, this is an administrative claim-based analysis with potential missing data and erroneous coding. However, the claims algorithm used in this study has captured HF patients with 98% specificity, when compared with a telephone survey of patients in a previously published study (Rector et al., 2004). Although administrative claims data are not perfect, it allows for studies on large populations in "real-world" settings; this study would have been prohibitively costly and time consuming using a chart review method. Lastly, unmea-

**Table 3. Impact of Receipt of an ACEI/ARB on Total Healthcare Cost in the Following Year among Heart Failure Patients**

	Healthcare Cost Coefficient Estimate (95% CI) ( <i>n</i> = 2,396)
Received ACEI/ARB (reference: no)	0.06 (−0.06–0.18)
Age (reference: <50 years)	
50–64 years	0.36 (0.14–0.57) **
≥ 65 years	0.66 (0.46–0.86) ***
Female (reference: male)	−0.001 (−0.12–0.12)
≥ 10 drug types (reference: <10 drug types)	0.66 (0.48–0.83) ***
Seen by a cardiologist (reference: no)	0.01 (−0.10–0.12)
Elixhauser comorbidity score	0.04 (0.01–0.08) *
Baseline healthcare cost	0.26 (0.21–0.32) ***
Year (reference: 2005)	
2000	−0.10 (−0.26–0.05)
2001	−0.09 (−0.24–0.06)
2002	−0.04 (−0.19–0.11)
2003	−0.02 (−0.17–0.12)
2004	0.04 (−0.11–0.18)

*Note.* ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker.  
 \* *p* value < .05,  
 \*\* *p* value < .01,  
 \*\*\* *p* value < .001.

sured factors such as stage of HF, left ventricular ejection fraction, body mass index, and smoking status that are unavailable in claims data, may have impacted healthcare utilization and healthcare cost. In particular, it is not possible to discriminate between systolic and diastolic HF using administrative claims data. If the distinction between these two types of HF was able to be made, there is the possibility of providing an ACEI/ARB to be cost saving.

In conclusion, this “real-world” study suggests that prescribing ACEIs/ARBs to patients with HF was effective in reducing hospitalizations and emergency department visits without a significant increase in total healthcare costs. Incentivizing the receipt of ACEIs/ARBs in these patients may be a suitable target for P4P programs, disease management programs, or newer complementary frameworks, such as value-based insurance design.

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