

# Adherence to Guideline-Recommended Adjunctive Heart Failure Therapies Among Outpatient Cardiology Practices (Findings from IMPROVE HF)

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Although previous studies have documented adherence with certain established heart failure (HF) quality metrics in outpatient cardiology practices, the extent to which there is conformity with other evidence-based, guideline-driven quality metrics in outpatients with HF is unknown. IMPROVE HF is a prospective cohort study designed to characterize the current management of patients with chronic HF and left ventricular ejection fraction  $\leq 35\%$  in outpatient cardiology practices. We evaluated baseline data for conformity with adjunctive HF therapies including pneumococcal vaccination, hydralazine/isosorbide dinitrate (HYD/ISDN) for Black patients, statin therapy, antiplatelet therapy, smoking-cessation counseling, low-density lipoprotein cholesterol levels ( $< 100$  mg/dl), and systolic blood pressure decrease (all patients  $< 140$  mm Hg or [optimal]  $< 130$  mm Hg). Baseline data were available for 15,381 patients attending 167 cardiology practices. Patient characteristics included a median age 70 years, 71.0% men, 9.1% Black patients, 65.2% with ischemic HF cause, and 61.7% with a history of hypertension. Mean adherences or documentations of adherence were only 7.3% for HYD/ISDN and 1.0% for pneumococcal vaccination. Adherence to other adjunctive therapies ranged from 27.4% to 82.0% but none of the adjunctive treatment interventions were associated with high levels of adherence. Conformity with guideline-recommended, adjunctive HF therapies is deficient in the management of outpatients with HF. Critical gaps in documentation or delivery of care exist, especially for the use of pneumococcal vaccination and HYD/ISDN. In conclusion, improved processes of care, better documentation, and/or increased measures to promote adherence to all primary and adjunctive therapies for HF are needed. © 2010 Elsevier Inc. All rights reserved. (Am J Cardiol 2010;105:255–260)

Treatment of patients with heart failure (HF) has benefited from the discovery of interventions that led to evidence-based guidelines.<sup>1–4</sup> Current research demonstrates improved, but not optimal, adherence to certain evidence-based, guideline therapies for inpatients with

symptomatic HF.<sup>5–7</sup> Evaluation of care provided to patients with HF in outpatient settings demonstrates a high level of adherence to some, but not all, American College of Cardiology/American Heart Association class I indicated therapies for HF.<sup>8–11</sup> Additional guideline-recommended interventions have been established for the treatment of HF including the use of isosorbide dinitrate plus hydralazine (HYD/ISDN) for Black patients, optimal control of blood pressure, lipid treatment, antiplatelet therapies for patients with concomitant coronary artery disease (CAD), and pneumococcal vaccinations.<sup>1–4</sup> The extent to which these other guideline-recommended, adjunctive therapies have been integrated in the care of outpatients with HF has not previously been studied. Baseline data from the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) provided the opportunity to evaluate the degree to which outpatient HF care was consistent with the guideline recommendations for adjunctive therapies.

## Methods

IMPROVE HF is a prospective cohort study designed to characterize management of patients diagnosed with HF or

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**Table 1**  
Baseline Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) patient demographic and clinical characteristics

Characteristic	Study Population (n = 15,381)
Age (years), median (IQR)	70.0 (60–79)
<65	5,307 (34.5%)
65–76	5,176 (33.7%)
>76	4,791 (31.1%)
Men	10,925 (71.0%)
White	6,362 (41.4%)
Black	1,398 (9.1%)
Not documented or missing	13,431 (47.8%)
Insurance type	
Medicare	9,240 (60.1%)
Medicaid	549 (3.6%)
Private	3,822 (24.8%)
Other	544 (3.5%)
Not documented	975 (6.3%)
None	187 (1.2%)
Heart failure cause, ischemic	10,025 (65.2%)
History of atrial fibrillation	4,732 (30.8%)
History of diabetes	5,229 (34.0%)
History of hypertension	9,484 (61.7%)
Previous myocardial infarction	6,061 (39.4%)
History of chronic obstructive pulmonary disease	2,530 (16.4%)
History of coronary artery bypass grafting	4,746 (30.9%)
History of peripheral vascular disease	1,739 (11.3%)
History of depression	1,349 (8.8%)
NYHA class	
I	3,097 (20.1%)
II	4,022 (26.1%)
III	2,720 (17.7%)
IV	383 (2.5%)
Not documented	5,159 (33.5%)
Left ventricular ejection fraction (%), median (IQR)	25.0 (20–30)
Systolic blood pressure (mm Hg), median (IQR)	120 (108–130)
Diastolic blood pressure (mm Hg), median (IQR)	70 (60–80)
Heart rate at rest (beats/min), median (IQR)	71 (64–80)
Rales on most recent examination	567 (3.7%)
Edema on most recent examination	3,030 (19.7%)
Sodium (mEq/L), median (IQR)	140 (137–141)
Serum urea nitrogen (mg/dl), median (IQR)	22 (16–30)
Creatinine (mg/dl), median (IQR)	1.2 (1.0–1.6)
$\beta$ -natriuretic peptide (pg/ml), median (IQR)	383.7 (158–877)
QRS duration (ms), median (IQR)	124.0 (100–156)
QRS duration >120%	5,773 (52%)
ACEI/ARB*	11,268/14,161 (79.6%)
$\beta$ blocker*	12,006/13,968 (86.0%)
Aldosterone antagonist use*	905/2,505 (36.1%)
Anticoagulation for atrial fibrillation use*	2,939/4,308 (68.2%)
Cardiac resynchronization therapy use*	533/1,373 (38.8%)
Implantable cardioverter–defibrillator/cardiac resynchronization therapy device and defibrillator use*	3,659/7,221 (50.7%)

\* Based on eligible patients without contraindications.

ACEI/ARB = angiotensin-converting enzyme inhibitor and/or angiotensin receptor blocker; IQR = interquartile range; NYHA = New York Heart Association.

previous myocardial infarction (MI) and left ventricular systolic dysfunction in outpatient cardiology (single specialty or multispecialty) practice settings. The objectives,

**Table 2**  
Baseline Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) practice characteristics

Characteristic	Practice Sites (n = 167)
Census region	
South	65 (38.9%)
Northeast	54 (32.3%)
Central	26 (15.6%)
West	20 (12.0%)
Outpatient practice setting*	
University, teaching	13 (7.8%)
Nonuniversity, teaching	36 (21.6%)
Nonuniversity, nonteaching	108 (64.7%)
Multispecialty	40 (24.0%)
Electronic health record	
Paper only	80 (47.9%)
Paper and electronic health record combined	37 (22.2%)
Electronic health record only	50 (29.9%)
Heart failure nurses (>1 FTE APN)	58 (34.7%)
Electrophysiologist in practice	105 (62.9%)
Interventionalist in practice	146 (87.4%)
Heart failure clinic in practice	69 (41.3%)
Number of cardiologists in practice, mean/median (IQR)	12.0/9.0 (6–15)
Number of patients with heart failure managed annually by practice, mean/median (IQR)	32,13.5/1,837.5 (550–4,000)

\* Outpatient practice setting is missing for 5.9% of practices.

APN = advanced practice nurse; FTE = full time equivalent. Other abbreviation as in Table 1.

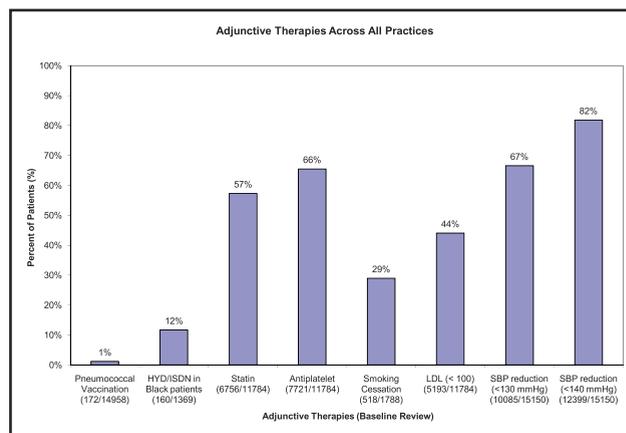


Figure 1. Proportions of patients receiving each of the adjunctive HF therapies is shown across all practice sites. Statin and antiplatelet therapy was indicated for patients with CAD, cardiovascular disease, or peripheral vascular disease. LDL = low-density lipoprotein; SBP = systolic blood pressure.

design, and detailed methods of IMPROVE HF have previously been published.<sup>12</sup> Patients were eligible for enrollment in IMPROVE HF if they were  $\geq 18$  years of age, had a primary or secondary diagnosis of HF or previous MI, and moderate-to-severe left ventricular dysfunction (LVD) confirmed qualitatively or by a quantitative LV ejection fraction  $\leq 35\%$ . LV ejection fraction  $\leq 35\%$  was measured by the most recent echocardiogram, nuclear multiple-gated acquisition scan, contrast ventriculogram, or magnetic resonance imaging scan. Patients were excluded from the study cohort

Table 3  
Eligible patients treated with adjunctive therapy

Adjunctive Therapy (eligible patients)	Mean $\pm$ SD for Sites	Median for Sites	25th, 75th Percentiles for Sites	10th, 90th Percentiles for Sites	Cumulative for Entire Cohort
Pneumococcal vaccination (n = 14,958)	1.0 $\pm$ 3.30%	0.0%	0.0%, 0.0%	0.0%, 2.5%	172 (1.1%)
HYD/ISDN for Black patients (n = 1,369)	7.3 $\pm$ 14.76%	0.0%	0.0%, 8.3%	0.0%, 25.0%	160 (11.7%)
Statin* (n = 11,784)	57.1 $\pm$ 13.86%	56.9%	51.0%, 65.6%	40.0%, 73.3%	6,756 (57.3%)
Low-density lipoprotein <100 mg/dl (n = 11,784)	44.8 $\pm$ 17.18%	45.3%	33.7%, 57.1%	21.4%, 67.5%	5,193 (44.1%)
Antiplatelet (n = 11,784)	64.6 $\pm$ 12.91%	65.7%	60.4%, 72.0%	50.9%, 77.6%	7,721 (65.5%)
Smoking cessation (n = 1,788)	27.4 $\pm$ 23.22%	25.0%	8.3%, 40.0%	0.0%, 61.1%	518 (29.0%)
Systolic blood pressure <140 mm Hg (n = 15,150)	82.0 $\pm$ 6.00%	82.5%	78.7%, 86.0%	74.5%, 88.9%	12,399 (81.8%)
Systolic blood pressure <130 mm Hg (n = 15,150)	66.6 $\pm$ 7.79	67.2%	61.5%, 71.2%	57.0%, 76.6%	10,085 (66.6%)

\* Statin and antiplatelet therapy for CAD, cardiovascular disease, or peripheral vascular disease.

if they were not expected to survive  $\geq 12$  months due to medical conditions other than HF or if they had undergone heart transplantation surgery. Patients with preserved systolic function or without measurements of LV ejection fraction were also excluded.

Baseline patient data were collected by trained chart abstractors and included demographic and clinical characteristics, medical history, previous treatments, results from laboratories and diagnostic tests, current treatments for HF, and any contraindications or documentation of other reasons (e.g., economic, social, religious reasons, noncompliance, and other reasons for refusal) for not prescribing evidence-based therapies. Self-identified race was collected by administrative or medical staff and abstracted as documented in the medical record. Inter-rater variability of chart reviewers was measured and demonstrated a high level of consistency ( $\kappa = 0.82$ ). In addition, 1.7 automated data-quality checks were performed for each data field and data quality was monitored and reports generated monthly. The registry co-ordinating center is Outcome Sciences, Inc. (Cambridge, Massachusetts). The IMPROVE HF registry and this study are sponsored by Medtronic, Inc. (Minneapolis, Minnesota). The authors are solely responsible for the design and conduct of this study, all study analyses, drafting and editing of the report, and its final contents.

Adjunctive care measurements were developed for HF therapies with American College of Cardiology/American Heart Association class IIA recommendations and for therapies to manage co-morbid conditions or related risks with American College of Cardiology/American Heart Association class I recommendations.<sup>2,3</sup> The following adjunctive measurements were defined and included in this analysis: pneumococcal vaccination for all patients; HYD/ISDN in Black patients with HF and LVD; statin use for patients with HF and CAD, cerebral or peripheral vascular disease, or LVD after MI; low-density lipoprotein cholesterol levels <100 mg/dl in patients with HF and CAD, cerebral or peripheral vascular disease, or LVD after MI; antiplatelet therapy (aspirin or clopidogrel) for patients with HF and CAD, cerebral or peripheral vascular disease, or LVD after MI; smoking-cessation counseling for current smokers with HF or LVD after MI; conventional blood pressure control to decrease systolic blood pressure to <140 mm Hg in patients with HF or LVD after MI; and newer optimal

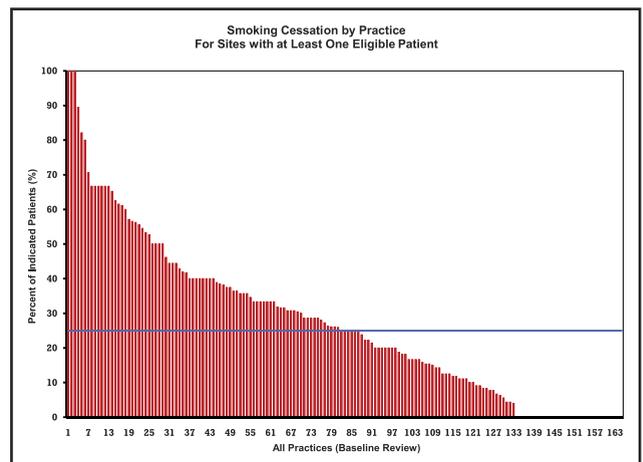


Figure 2. Smoking cessation by practice for sites with  $\geq 1$  eligible patient, with median percentage for sites (solid blue line).

control of blood pressure to decrease systolic blood pressure <130 mm Hg in patients with HF or LVD after MI.

This analysis included all baseline data entered into the registry from May 2005 to June 2007 and included 15,381 patients from 167 university-affiliated and nonaffiliated cardiology and multispecialty practices located in the United States. A representative sample of medical records was screened to yield an average of 90 eligible patients from each practice using the methods described in the design publication.<sup>12</sup> The present analysis of conformity with adjunctive care metrics was prespecified in the study protocol. Each cardiology practice received previous approval to participate in the study from a local or central institutional review board or a waiver to disclose patient health information in compliance with the Health Insurance Portability and Accountability Act.

All statistical analyses were performed by independent biostatisticians contracted by Outcome Sciences, Inc. Data are reported as the number and frequency of patients currently managed using each of the 7 adjunctive therapies described earlier. Data were analyzed per practice for mean, SD, median, 25th and 75th percentiles of conformity, and 10th and 90th percentiles of conformity for each measurement. Evaluation of conformity included only patients documented to be eligible to receive a specific adjunctive therapy.

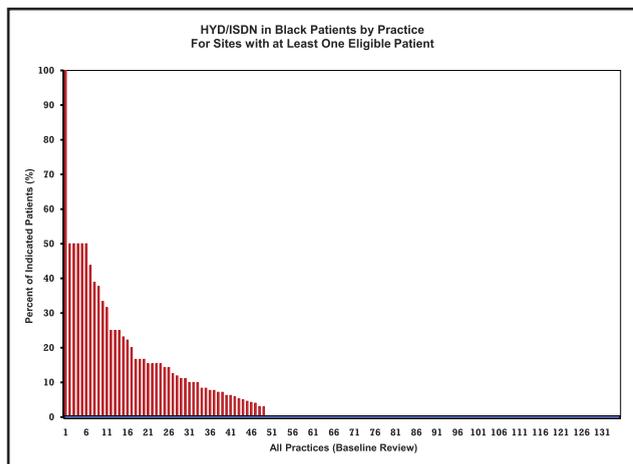


Figure 3. HYD/ISDN therapy in Black patients by practice for sites with  $\geq 1$  eligible patient, with median percentage for sites (solid blue line).

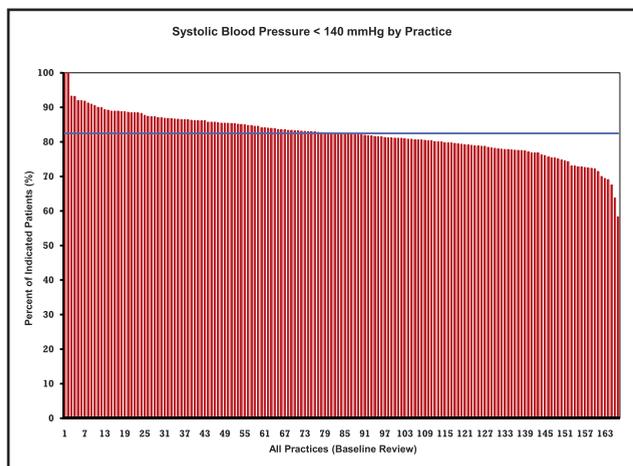


Figure 4. Systolic blood pressure <140 mm Hg by practice, with median percentage for sites (solid blue line).

## Results

Baseline demographic and clinical characteristics of enrolled patients are listed in Table 1. Mean and median ages were 69 and 70 years, with 71% men, and, where a racial designation was available, 9.1% were Black. Participating practice characteristics are listed in Table 2. All regions of the country were represented. Most participating practices were nonacademic (64.7%), 41.3% had established HF clinics, and 52.1% reported use of electronic health records.

Rates of adherence to guideline-recommended, adjunctive HF therapies are presented in Figure 1 and Table 3. The highest conformity was evident for control of systolic blood pressure <140 mm Hg with a mean adherence rate of 82.0% for practices. Remarkably, median practice adherence rates for pneumococcal vaccination and HYD/ISDN were 0.0% for the 2 care measurements and mean practice adherence rates for pneumococcal vaccination and HYD/ISDN therapy were 1.0% and 7.3%, respectively (Table 3).

Adherence to adjunctive HF therapies varied substantially among practices (Figures 2, 3, and 4, Table 3). Comparisons of adherence rates by practices for each adjunctive therapy ranged from 0.0% to 2.5% for pneumococcal vac-

ination to 74.5% to 88.9% for systolic blood pressure <140 mm Hg at the 10th and 90th percentiles, respectively. More than 71% of practices failed to administer or document administration of HYD/ISDN treatment for eligible Black patients in the absence of documented contraindications or intolerance. With the exception of pneumococcal vaccination, adherence to all adjunctive therapies was significantly lower for patients with HF compared to rates of adjunctive therapies for patients with LDV after MI ( $p < 0.001$  for all comparisons; Table 4).

## Discussion

These results from IMPROVE HF provide new insights about patterns of care for patients with HF who are followed in outpatient cardiology practices. These findings postdate release of the updated national HF guidelines and can be considered to reflect the current standards of care for patients with ambulatory HF. Unlike clinical trials, which have multiple exclusion criteria for enrollment and care guidelines established by study protocols, this registry reflects real-world management in a variety of cardiology practices from all regions of the United States.

These data are among the first to evaluate adherence to adjunctive therapies for treatment of HF in ambulatory outpatients. The findings we report are reasons for concern because even those therapies for which adherence is higher still reflect a 15% to 40% gap in care. Even more disconcerting is the low adherence rate or documentation of adherence to HYD/ISDN therapy for Blacks. Published data clearly confirm the adjunctive benefit of HYD/ISDN for Blacks.<sup>13</sup> When given in conjunction with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and  $\beta$  blockers, HYD/ISDN is associated with an additional 43% decreased risk of death, decreased rates of hospitalization for HF, and improved quality of life.<sup>13</sup> However, these data and other hospital-based registry data confirm poor uptake of this evidence-based therapy for at-risk patients.<sup>14</sup> The current data are confounded by a significant amount of missing information on patient race. To accommodate this short-coming, the data were evaluated as a function of documented race and as non-White. The 2 assessments yielded evidence of extremely low adherence rates to treatment of eligible patients with HYD/ISDN. It is unclear whether this represents a lack of awareness regarding the potential benefit of this therapy for Black patients with HF or a circumspect view of the published data. Nevertheless, an important concern regarding disparate health care must be raised because an otherwise reasonable and effective treatment intervention is not used in an at-risk special population. Similarly, the benefit of pneumococcal vaccination is incontrovertible yet these data suggest poor adherence or documentation of this adjunctive therapy. Because administration of pneumococcal vaccination frequently occurs in hospital or primary care practice settings, this finding may reflect a lack of continuity with inpatient and outpatient health records. These important deficits in care suggest opportunities for performance improvement initiatives.

Adherence to standard and optimal control of blood pressure metrics is reasonable but not optimal. Published

Table 4  
Conformity of practices to recommended adjunctive heart failure therapies

HF Therapy	Cumulative for Patients With HF	Cumulative for Patients With LVD After MI	p Value
Pneumococcal vaccination	1.2% (103/8,949)	1.2% (69/5,800)	1.000
Statins	52.0% (2,934/5,639)	62.6% (3,753/5,992)	<0.001
Antiplatelet therapy	60.3% (3,398/5,639)	70.7% (4,236/5,992)	<0.001
Systolic blood pressure <140 mm Hg	80.8% (7,230/8,949)	83.8% (5,024/5,992)	<0.001
Systolic blood pressure <130 mm Hg	65.3% (5,846/8,949)	68.8% (4,125/5,992)	<0.001
Low-density lipoprotein <100 mg/dl	40.0% (2,254/5,639)	48.4% (2,899/5,992)	<0.001

\*Statin and antiplatelet therapy for CAD, cardiovascular disease, or peripheral vascular disease.

data regarding blood pressure control and improvement in symptomatic HF are limited and not persuasive. For example, the African-American Heart Failure Trial (A-HeFT) trial reported that >60% of HF cases were attributable to hypertension. However, overall blood pressure decrease was only 2 to 3 mm Hg, which was not sufficient to explain the profound decreases in mortality.<sup>13</sup> Other randomized, controlled trials have not provided convincing evidence that decreases in blood pressure in response to evidence-based therapy are associated with improved outcomes for patients with HF.<sup>1-3,15</sup> Data are more compelling for the prevention of HF with blood pressure control therapies. Decrease of systolic blood pressure in the Systolic Hypertension in the Elderly Program (SHEP) trial led to a  $\geq 50\%$  decrease in the incidence of HF, although patients did not achieve goal blood pressure decreases.<sup>16</sup> Similarly, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) confirmed a decrease in progression to HF in patients treated with a thiazide-based regimen.<sup>17</sup> Thus, it is reasonable but not yet proved that vigorous control of blood pressure will benefit patients with established hypertension and HF.

Several important studies have demonstrated that statin therapy independent of lipid-lowering effects may be associated with improved outcomes in HF.<sup>18</sup> However, the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA) evaluated the benefit of adjunctive statin therapy for patients with known ischemic heart disease, decreased ejection fraction, and clinical HF and reported no survival benefit and only a modest decrease in morbidity.<sup>19</sup> Importantly, the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico-Heart Failure (GISSI-HF) trial evaluated patients with HF from different causes who were already receiving reasonable medical therapy and demonstrated no benefit of adjunctive statin therapy.<sup>20</sup>

Although there has been debate regarding the benefit of aspirin for patients with HF,<sup>21,22</sup> the benefit of aspirin in the setting of CAD cannot be overstated.<sup>23,24</sup> However, there are no prospective trials that have specifically evaluated the benefit of adjunctive aspirin for HF. There is concern that the use of aspirin in HF may be problematic because of the inhibition of prostaglandin synthesis and subsequent production of endogenous vasodilators.<sup>21,22</sup> However, this concern has not been documented in practice or confirmed in clinical trials. Given the significant presence of CAD in patients with HF, this intervention appears warranted.

The wide variations in care across practices in this study may reflect differences in training, familiarity with guide-

lines, and variations in implementation of tools and systems to ensure that recommended care is provided. These variations may also reflect differences in documentation of care that was actually provided. Furthermore, documentation of current HF symptoms, contraindications, intolerances, and patient reasons and physician reasons for not providing guideline-recommended adjunctive therapies or reaching guideline-recommended blood pressure and low-density lipoprotein targets may have varied across practices. The data presented are baseline data and further study of the uptake of these adjunctive therapies is pending serial assessments within IMPROVE HF at 6 and 18 months by practice and 12 and 24 months by patients. Evidence that a process of care intervention improves the documentation or actual adherence to these adjunctive therapies would suggest that more widespread adoption of this or other process-of-care improvement strategies should be considered in outpatient cardiology treatment paradigms.

It is important to recognize certain limitations in the nonrandomized nature of the registry-based IMPROVE HF information. Data were collected by medical chart review and are dependent on the accuracy and completeness of documentation and abstraction, particularly because eligibility for care metrics is based on this documentation. Missing data represent another potential limitation. In addition, observer error is always a concern in large registry databases. Race was not consistently recorded so statements regarding care of patients based on race should be qualified. However, given the magnitude of nonadherence, the statements made are qualitatively, if not also quantitatively, correct. Documentation of adherence is a concern and for certain adjunctive measurements, the primary source of documentation is likely to be the inpatient record. An absence of continuity between inpatient and outpatient medical records is a global concern and impedes longitudinal quality assessment, which will be important as quality-driven initiatives are integrated into clinical practice. These findings may not apply to practices that differ from IMPROVE HF with respect to patient and practice characteristics. Larger or smaller gaps and variation in the use of adjunctive therapies for patients with HF may exist among different types of outpatient practices in the United States. However, these findings confirm the potential need and benefit of a performance improvement intervention that targets the most highly accepted guideline-recommended therapies and other important adjunctive treatments to improve outpatient care of patients with HF.

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