Reduced Ejection Fraction/Systolic Heart Failure: A Real-World Case Study Using Electronic Health Records

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### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ACC</td>
<td>American College of Cardiology</td>
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<td>ACCF</td>
<td>American College of Cardiology Foundation</td>
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<tr>
<td>ACEI</td>
<td>Angiotensin-Converting Enzyme Inhibitor</td>
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<td>AHA</td>
<td>American Heart Association</td>
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<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blocker</td>
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<td>ARNI</td>
<td>Angiotensin Receptor-Nephrilysin Inhibitor</td>
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<tr>
<td>BNP</td>
<td>B-Type Natriuretic Peptide</td>
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<td>EF</td>
<td>Ejection Fraction</td>
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<td>EHR</td>
<td>Electronic Health Record</td>
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<tr>
<td>ED</td>
<td>Emergency Department</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FHIR</td>
<td>Fast Healthcare Interoperability Resource</td>
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<td>GDMT</td>
<td>Guideline-Directed Medical Therapy; Guideline-Directed Management and Therapy</td>
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<td>GWTG</td>
<td>Get with the Guidelines</td>
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<td>HCP</td>
<td>Healthcare Provider</td>
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<td>HITRUST</td>
<td>Health Information Trust Alliance</td>
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<td>HF</td>
<td>Heart Failure</td>
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<td>HFP EF</td>
<td>Heart Failure with Preserved Ejection Fraction</td>
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<td>HFR EF</td>
<td>Heart Failure with Reduced Ejection Fraction</td>
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<tr>
<td>I$_f$</td>
<td>Hyperpolarization-Activated Pacemaker Current; “funny” current</td>
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<tr>
<td>IVB</td>
<td>Ivabradine</td>
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<td>MRA</td>
<td>Mineralocorticoid Receptor Antagonist</td>
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<td>NLP</td>
<td>Natural Language Processing</td>
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<tr>
<td>NT-proBNP</td>
<td>N-Terminal Pro-B-Type Natriuretic Peptide</td>
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<td>NYHA</td>
<td>New York Heart Association</td>
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<td>RCT</td>
<td>Randomized Clinical Trial</td>
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<td>RWD</td>
<td>Real-World Data</td>
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<td>RWE</td>
<td>Real-World Evidence</td>
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<tr>
<td>SGLT-2</td>
<td>Sodium Glucose Cotransporter-2</td>
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EXECUTIVE SUMMARY

Heart failure is a complex clinical syndrome arising from structural or functional impairments of ventricular filling or ejection of blood. With its increasing prevalence and the aging of the population, the economic burden of heart failure on the US healthcare system is substantial and continues to increase. High morbidity and mortality make heart failure a significant concern for patients and their families. Management is challenging, especially in the presence of comorbidities, which can be risk factors for developing heart failure as well as complicating factors in established heart failure. The gaps in use and dosing of evidence-based, guideline-recommended therapies suggest a care deficit exists such that treatment remains suboptimal for a significant number of heart failure patients.

This paper provides insight into current knowledge regarding heart failure, with an emphasis on systolic (i.e., reduced ejection fraction) heart failure and guideline-directed medical therapy (GDMT). We consider how real-world evidence derived from de-identified patient information available in electronic health record (EHR) platforms may be leveraged to inform and advance appropriate care plans in heart failure. With a focus on new pharmacotherapies, a retrospective case study using real-world data from the EHR platform Practice Fusion, a Veradigm™ offering, demonstrates that nearly one third of ambulatory heart failure patients were not receiving at least one GDMT. The study also indicates that new medications specifically approved for the treatment of systolic heart failure may be underutilized despite being important advances in heart failure care management. Future studies that leverage real-world evidence from multiple electronic platforms may provide insight into patient quality of life, hospitalizations, and survival in heart failure.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome arising from structural or functional impairment of ventricular filling or ejection of blood (Yancy et al, 2013). Between 2011 and 2014, the number of Americans estimated to be living with HF was 6.5 million (Benjamin et al, 2017). The prevalence of HF continues to rise; by 2030, 3% (>8 million) of the US population is conservatively projected to receive a diagnosis of HF (Heidenreich et al, 2013). The increasing prevalence of HF reflects rising rates of obesity, hypertension, and diabetes in the general population, as well as increased survival rates for patients who are successfully treated for myocardial infarction (Huffman et al, 2013). The incidence of HF rises with age; more than 60% of patients with HF are 65 years or older (Heidenreich et al, 2013; Kilgore et al 2017).

With its growing prevalence and the aging of the population, the economic burden imposed by HF on the US healthcare system is substantial and continues to increase.

- Lifetime costs of HF are mostly due to hospitalizations; more Medicare dollars are spent on HF than on any other diagnosis (Dunlay et al, 2011).
- Total costs (direct and indirect) for HF are anticipated to increase from $30.7 billion in 2012 to nearly $70 billion in 2030 (Heidenreich et al, 2013). If costs attributable to comorbid condi-
tions are included, the projected cost of treating patients with HF increases 3-fold, with $160 billion in direct costs alone (Heidenreich et al, 2013).

- According to the American Heart Association (AHA), preventing HF and improving efficiency of care are critical to reducing use of limited healthcare resources (Heidenreich et al, 2013).

**HF is a significant concern for patients and their families owing to its high morbidity and mortality.**

- As a chronic disorder characterized by acute exacerbations that require intervention in hospital settings, HF is the most frequent cause of hospitalization in patients aged 65 years and older (Roger, 2013).

- After a first hospitalization, prognosis of HF worsens. A longitudinal study that evaluated registry and Medicare-linked data for nearly 40,000 patients who had been hospitalized for HF between 2005 and 2009 reported an elevated risk for cardiovascular and HF hospital readmission, with very poor survival (75% mortality) at 5 years (Shah et al, 2017).

- Multiple hospitalizations were common in a community study that evaluated a random sample of HF cases and all hospitalizations following a HF diagnosis, with 83.1%, 66.9%, 53.6%, and 42.6% of patients hospitalized at least once, two or more, 3 or more, or 4 or more times, respectively (Dunlay et al, 2009).

- HF was listed as a contributing cause on 1 in 8 death certificates in 2009 (Benjamin et al, 2017).

**Comorbidities are common in patients with HF, and concurrent management is challenging.**

- Comorbidities are risk factors for developing HF and complicating factors in established HF (Bozkurt et al, 2016).

- It is estimated that nearly three-quarters of patients with HF have at least one comorbid condition; more than one half of Medicare patients with HF have at least five chronic comorbidities (CardioSmart, 2018).

- Comorbid conditions are strongly associated with hospitalizations (Dunlay et al, 2009). Coronary artery disease (ischemia), arrhythmias, and hypertension are cardiovascular comorbidities for which patients with HF are hospitalized (Kilgore et al, 2017). Hypertension is highly associated with HF in six world regions, including North America (Khatibzadeh et al, 2017).

- In a community study, more than one-half of hospital readmissions following a diagnosis of HF were associated with non-cardiovascular diseases (Dunlay et al, 2009). Non-cardiovascular conditions associated with hospitalizations include diabetes mellitus, obesity, anemia, chronic obstructive pulmonary disease, kidney disease, and sleep disordered breathing (Mentz et al, 2014; Bozkurt et al, 2016).
TYPES OF HF

HF constitutes a final common pathway for disorders of myocardial, endocardial, pericardial, valvular, or vascular origin (Heidenreich et al., 2013; Yancy et al, 2013). Dyspnea and fatigue, which restrict the capacity for exercise, and fluid retention causing edema in the periphery and congestion in the lungs are common symptoms. Symptoms in most patients arise from left ventricular dysfunction (Yancy et al, 2013).

In the 2013 ACCF/AHA Guideline for the Management of Heart Failure, HF is defined according to the functional status, or ejection fraction (EF), of the left ventricle. EF is an important means of categorizing HF owing to differences in patient demographics, comorbidities, prognosis, and therapeutic response; moreover, most clinical trials specify EF thresholds in the inclusion criteria for patient selection. Notwithstanding EF status, abnormalities arising from diastolic and systolic dysfunction coexist in most patients (Yancy et al, 2013).

Two major HF phenotypes have been identified:

- HF with preserved EF (HFpEF) (EF ≥50%), also referred to as diastolic HF (Aurigemma and Gaasch, 2004; American Heart Association, 2018b; Yancy et al, 2013)
- HF with reduced EF (HFrEF) (EF ≤40%), also referred to as systolic HF (McMurray, 2010; American Heart Association, 2018a; Yancy et al, 2013).

HFpEF/Diastolic HF

In patients with diastolic HF, the heart contracts forcefully, and EF is preserved. Diastolic dysfunction, which arises from an inability of cardiac muscle to relax following contractions because of ventricular wall stiffening, is evident during rest, exertion, or stress (Redfield, 2016; Mayo Clinic, 2018). Atrial fibrillation is common, and mortality is often due to non-cardiovascular causes (Redfield, 2016; Mayo Clinic, 2018). Therapy is limited to reducing volume overload, treating comorbidities, and implementing strategies that improve exercise tolerance, prevent hospitalizations, and manage chronic disease (Redfield, 2016). While no studies have demonstrated reductions in mortality, use of angiotensin receptor blockers may reduce HF hospitalizations in this population (Bozkurt, 2018). Potential therapies for diastolic HF, such as sodium glucose cotransporter-2 (SGLT-2) inhibitors and a combination angiotensin receptor-neprilysin inhibitor (ARNI), are under investigation in randomized clinical trials (RCTs) (US National Library of Medicine, 2013; US National Library of Medicine, 2017a; US National Library of Medicine, 2018a).

Patients with borderline EFs (41% to 49%) straddle an intermediate zone; characteristics, treatment, and outcomes resemble those of patients with diastolic HF (Yancy et al, 2013).

HFrEF/Systolic HF

In patients with systolic HF, the left ventricle dilates, cardiac muscle is unable to contract forcefully, and EF is reduced (Yancy et al, 2013). At least one-half of patients with a diagnosis of HF have systolic HF; in two-thirds of these patients, coronary artery disease and its complications
(e.g., myocardial infarction) are primary causes (McMurray, 2010). Following myocardial injury, compensatory mechanisms such as

- increased heart rate, increased myocardial contractility, and peripheral vasoconstriction via activation of the sympathetic nervous system (SNS) and
- vasoconstriction, blood volume increase, and salt and water retention via activation of the renin-angiotensin-aldosterone system (RAAS)

increase cardiac output over the short term. However, long-term neurohormonal changes lead to continued pathologic ventricular remodeling, worsening of symptoms and functional capacity, decompensation and hospitalization, and pump failure with premature death (Jackson et al, 2000; McMurray, 2010; Healio, 2018).

For patients with systolic HF, substantial clinical evidence is available to guide treatment, with information on pharmacotherapies, devices, biomarkers, and diagnostic and care strategies continually being updated in treatment guidelines and consensus decision publications (Yancy et al, 2013; Yancy et al, 2016; Yancy et al, 2017; Baliga, 2017; Yancy et al, 2018). Potential treatments, including SGLT-2 inhibitors and omecamtiv mecarbil, a cardiac myosin activator, are currently in late-stage development (US National Library of Medicine, 2017b; US National Library of Medicine, 2017c; US National Library of Medicine, 2017d; US National Library of Medicine, 2018b).

Clinical evidence has emerged for a subset of patients with improvement in EF (Yancy et al, 2013; Yancy et al, 2018). Patients with recovered heart function may require HF treatment indefinitely, given the findings of an open-label, randomized pilot study of patients with systolic HF due to dilated cardiomyopathy. Of those patients who had attained improved ventricular function and asymptomatic status following pharmacologic treatment, 44% (11/25) relapsed within six months of withdrawal of therapy compared with no patients (0/26) who continued therapy (Halliday et al, 2018).

MANAGEMENT OF HF

The goals of HF treatment are threefold: to reduce symptoms, to decrease hospitalization rates for acute exacerbations, and to prevent premature death (McMurray, 2010). A functional classification devised by the New York Heart Association (NYHA) affords a means of monitoring symptoms and conveying information regarding HF presence and severity (Bozorgnia and Mather, 2015; Yancy et al, 2013). Healthcare providers (HCPs) aim to keep patients in Class I (no limitation on physical activity; ordinary physical activity does not cause HF symptoms) or II (slight limitation; comfortable at rest, but ordinary physical activity results in HF symptoms) or to increase care levels for functional classes III (marked limitation; comfortable at rest, but less than ordinary activity causes HF symptoms) and IV (unable to carry on any physical activity without symptoms of HF at rest) (Bozorgnia and Mather, 2015; Yancy et al, 2013).

Management of HF requires a multidisciplinary approach, with a focus on care identification and coordination, management of comorbidities, individualization of therapy, and patient education (Bozkurt, 2018). In conjunction with multidisciplinary management, quality initiatives (i.e., clinical
decision support tools, reminder systems, chart audits, benchmarked reports, and educational outreach) may promote uniform implementation of evidence-based therapy and patient self-care, with better clinical outcomes (Atherton, 2012; Fonarow et al, 2010). Disease management programs and telemonitoring may reduce hospital readmissions and mortality (Chavey et al, 2017).

In addition to pharmacologic therapy, implantable devices (i.e., cardioverter-defibrillators and biventricular pacemakers) may improve functionality and reduce mortality in eligible patients (Yancy et al, 2013; Chavey et al, 2017). Patient education and lifestyle modification, such as exercise training or regular physical activity to improve functional status and sodium restriction to reduce congestion, are also recommended (Yancy et al, 2013). However, a recent systematic review of randomized trials investigating the effects of reduced salt intake found limited evidence for clinical improvement in ambulatory HF patients and inconclusive evidence for improvement in hospitalized HF patients, prompting calls for well-controlled, high-quality studies that address the sodium issue as well as other dietary gaps in HF care (Mahtani et al, 2018; Yancy, 2018).

**HFrEF/Systolic HF and Guideline-Directed Medical Therapy (GDMT)**

The 2013 ACCF/AHA Task Force on Practice Guidelines assigned the term “guideline-directed medical therapy” to describe optimal medical therapy for patients with HF (Yancy et al, 2013). Optimal therapy has been defined in the treatment guidelines, focused updates, and consensus decision communications (Yancy et al, 2013; Yancy et al, 2016; Yancy et al, 2017; Baliga, 2017; Yancy et al, 2018). In the 2013 guideline, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and beta-blockers (specifically, bisoprolol, carvedilol, sustained-release metoprolol succinate) were named GDMT for patients with systolic HF (HFrEF stage C [i.e., structural heart disease with prior or current symptoms of HF], with a NYHA Class I-IV level of functional limitation for physical activity) (Yancy et al, 2013). Other pharmacotherapies designated GDMT were loop diuretics (for volume overload, NYHA class II-IV), hydral nitrates (for persistently symptomatic African Americans, NYHA class III-IV), and aldosterone antagonists (provided estimated creatinine >30 mL/min and potassium <5.0 mEq/dL, NYHA class II-IV).

In the 2017 Focused Update of the 2013 ACCF/AHA Guidelines, the definition of GDMT evolved to “guideline-directed management and therapy” (Yancy et al, 2017). GDMT currently includes clinical evaluation, diagnostic testing, pharmacotherapies, and procedures, with recommendations limited to drugs, devices, and treatments that are approved for use in the US (Yancy et al, 2017). GDMT is associated with improvements in survival and reduced hospitalization in patients with systolic HF (Yancy et al, 2013; Yancy et al, 2016).

**HFrEF/Systolic HF and New Pharmacotherapies**

Two new categories of pharmacotherapies for HF, introduced in the 2016 ACC/AHA/HFSA Focused Update as complementary to previously established pharmacological and device-based therapies, are important advances in the evolution of HF patient care (Yancy et al, 2016). Descriptions of and recommendations for these FDA-approved pharmacotherapies – sacubitril/valsartan, an angiotensin receptor-neprilysin inhibitor (ARNI) and ivabradine (IVB), a sinoatrial node blocker – for patients with systolic HF are provided in the accompanying textbox.
Sacubitril/valsartan, a combination ARB/prodrug neprilysin inhibitor, was designed to minimize the risk of serious angioedema (McMurray et al, 2014). Neprilysin inhibitors potentiate the beneficial effects of natriuretic peptides, with resultant vasodilation and reductions in remodeling and hypertrophy (Bozkurt, 2018). Neprilysin inhibitor use is associated with increased RAAS activity; co-administration of the ARB valsartan counters vasoconstriction to reduce blood pressure (Bozkurt, 2018). A double-blind, placebo-controlled RCT (PARADIGM) that compared sacubitril/valsartan with enalapril in patients with systolic HF (EF <40%) was terminated early, according to pre-specified rules, owing to the superiority of sacubitril/valsartan in reducing the risk of death and hospitalization for these patients (McMurray et al, 2014). These results led to recommendations that ARNI replace ACEI or ARB, as appropriate and under specified conditions, to further reduce morbidity and mortality (Yancy et al, 2017). More recently, a second RCT conducted in patients with reduced ejection fraction who were hospitalized with acute decompensated HF demonstrated that sacubitril/valsartan was associated with greater reduction in the biomarker N-terminal pro-B-type natriuretic peptide (NT-proBNP), a clinical surrogate of efficacy, than enalapril therapy (Velazquez et al, 2018). For use of an ARNI, guideline-recommended indications include HFrEF with EF ≤40% and NYHA class II or III HF.

A second medication, ivabradine, a selective inhibitor of If current in the sinoatrial node, causes heart rate reduction (Yancy et al, 2017). For patients with normal sinus rhythm and a baseline heart rate greater than 70 bpm despite treatment with beta-blockers in a placebo-controlled RCT (SHIFT), treatment with ivabradine reduced the composite endpoint of cardiovascular death or HF hospitalization compared with placebo (Swedberg et al, 2010). In the 2017 Focused Update of the 2013 ACCF/AHA Guidelines, ivabradine is considered a beneficial therapy that reduces HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (EF ≤35%), who are receiving guideline-directed evaluation and management, including a beta-blocker titrated to the maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest (Yancy et al, 2017).

Systolic HF and Biomarkers

Natriuretic and vasodilatory peptides that are secreted by the heart, vasculature, kidney, and central nervous system in response to increased cardiac-wall stress inhibit RAAS and sympathetic activation (Owens et al, 2016). Treatment guidelines recommend BNP or NT-proBNP be measured and used to support clinical decision-making in diagnosing HF in ambulatory patients with dyspnea (Yancy et al, 2013). Additional recommendations in the 2017 focused update of HF guidelines indicate natriuretic peptides may be useful in screening for heart failure among high risk patients and in establishing prognosis (Yancy et al, 2017; Bozkurt, 2018).

2017 Expert Consensus Decision

To address gaps in clinical decision making, the ACC has addressed ten pivotal issues for systolic HF in a recent expert consensus document (see textbox).
TEN PIVOTAL ISSUES FOR HFrEF/SYSTOLIC HF

1. How to initiate and switch to new evidenced-based guideline-directed treatments
2. How to achieve optimal therapy given multiple drugs for HF, including augmented clinical assessment that may trigger changes to guideline-directed therapy (e.g., imaging, biomarkers, filling pressures)
3. When to refer to a specialist
4. How to address care coordination
5. How to improve adherence
6. What is needed in specific cohorts, including African Americans, frail, and elderly
7. How to manage cost of care
8. How to manage complexity
9. How to manage comorbidities
10. How to integrate palliative care and transition to hospice.

Yancy et al, 2018

In some patients, referral to a HF specialist (#3) may be necessary to ensure optimization of guideline directed therapy as well as implementation of advanced treatment options (e.g., mechanical circulatory support) (Yancy et al, 2013). Referrals may arise from a need for consultation or co-management. In a study that evaluated outpatient physician care following a visit to an emergency department (ED), early collaborative care was associated with increased use of medications, implementation of cardiovascular diagnostic testing, and better outcomes compared with primary care alone (Lee et al, 2010). Triggers for referral to a specialist or management program include new onset HF (for evaluation of etiology, evaluation and management of recommended therapies, and assistance in disease management) and features placing a patient with chronic HF at high risk, including persistent or worsening symptoms and adverse clinical events (Yancy et al, 2018). A study that monitored outcomes for patients who were hospitalized for acute decompensated heart failure concluded that care provided by cardiologists was associated with greater adherence to four core measures as well as significantly lower rates of adverse outcome than care provided by hospitalists and non-hospitalists (Uthamalingam et al, 2015).

Because nonadherence with GDMT is a causal factor in HF hospitalizations, HF guidelines recommend that patients at risk for hospitalization be evaluated and receive personalized education as part of an overall HF management strategy (Kapoor et al, 2016). Improvements in adherence (#5) require an understanding of factors related to the patient (e.g., poor health literacy), medical conditions and management of comorbidities, drug dosing and side effects, out-of-pocket costs and pharmacy access difficulties, and health system factors (e.g., silos of care, no automatic refills). Some proposed remedies include shifting language from “compliance” to “adherence,” initiating GDMT before hospital discharge, coordinating with other clinicians involved in patient care, and assessing adherence in patients at risk (e.g., carrying out drug reconciliation, monitoring pharmacy refills, reviewing drug and biomarker levels, and conducting home-based visits) (Baliga, 2017; Yancy et al, 2018).
Other factors complicate adherence. A recent study that recorded the extent of decongestion and the prescription status for neurohormonal therapy for HF patients at discharge from academic and community hospital settings demonstrated frequent deviation from treatment guidelines owing to hypotension, renal dysfunction, and inotrope use (Gilstrap et al, 2018). The authors conclude deviations in adherence to guidelines by clinicians may not reflect poor-quality care and suggest further study is required to determine best practices for these patients.

The presence of comorbidities (#9) worsens the severity of other comorbidities in a manner that is bi-directional, complicating prognosis. Although management of comorbidities may not specifically improve HF outcomes, such management is crucial to improving overall outcomes (Baliga, 2017; Yancy et al, 2018).

**RCTS AND REAL-WORLD EVIDENCE IN HF**

Randomized Clinical Trials or RCTs, the “gold standard” for determining the efficacy and safety of new pharmacotherapies and devices (Camm and Fox, 2017; Corrigan-Curry et al, 2018; Greene et al, 2018), provide the evidence base for GDMT. Conducted in specialized environments using well characterized protocols, RCTs employ restrictive enrollment criteria to control variability and ensure data quality (Sherman et al, 2016). Although RCTs are internally valid, they may not generalize to broader populations encountered in routine medical care. For example, patients with HF who are selected for RCTs have fewer comorbidities than patients in clinical practice (Colucci, 2018). Because these trials tend to include more men than women as well as patients who are younger than those in the general population, restrictions affecting external validity may be more obvious in HF trials (Roger, 2013). Finally, patients participating in RCTs may be more motivated and positively disposed to treatment than patients undergoing routine care (Camm and Fox, 2017).

According to the FDA, real-world evidence (RWE) is clinical evidence of the use and of the benefits or risks of medical products (Corrigan-Curay et al, 2018; US Food and Drug Administration, 2018a). Obtained outside of clinical research settings (Sherman et al, 2016), RWE may complement findings from RCTs by providing information on such variables as patient characteristics, clinical setting, and provider and health system processes, each of which influence treatment and outcomes (Sherman et al, 2016). RWE may be used to address gaps in care associated with patient and provider behavior, bringing to light the need for clinical decision support; it may also inform coverage decisions for medications, devices, and procedures (US Food and Drug Administration, 2018b). Sources of RWE include de-identified real-world data (RWD) that are routinely generated or collected from medical and prescription claims, patient and provider surveys, observational studies, and electronic health records (EHRs) (Sherman et al, 2016; Camm and Fox, 2017; US Food and Drug Administration, 2018a).
Clinical Registries

Clinical registries are observational studies without assignment to a specific intervention, in which uniform data are collected as part of usual care, or which incorporate elements of RWD (e.g., acquisition of hospital records or mortality data) (Jarow et al, 2017). Clinical registries have been used to gain insight into clinical presentation, patient care, and treatment outcomes for HF patients in the real world (Roger, 2013). An example of a large-scale, HF-specific registry is OPTIMIZE-HF, which enrolled more than 50,000 hospitalized patients with acute decompensated HF (Fonarow et al, 2004). OPTIMIZE-HF has since evolved into the Get with the Guidelines (GWTG) program, an in-hospital program for improving care through consistent adherence to the latest treatment guidelines (American Heart Association, 2018b). Findings from the OPTIMIZE-HF registry and Medicare linked claims data demonstrated that when patients with systolic HF, who were older and had more comorbidities than patients in HF RCTs, were treated according to ACC/AHA treatment guidelines, they had shortened hospital stays, reduced hospital re-admissions, and reduced mortality (Hernandez et al, 2009), confirming and extending the findings of a pivotal RCT (Packer et al, 2001). Similar findings were shown for the IMPROVE-HF clinical registry for outpatients with HF (Heywood et al, 2010; Fonarow et al, 2010).

In contrast to these earlier studies, results from the more recent CHAMP-HF, a registry of over 3,500 ambulatory US patients with chronic systolic HF, indicate that despite guidelines and quality improvement efforts, few patients (less than 1 in 4) are prescribed all three guideline-recommended drug types, and even fewer patients (1%) receive target doses of guideline-recommended medications (Greene et al, 2018). The gaps in use and dosing of evidence-based, guideline-recommended pharmacotherapies for systolic HF suggest a care deficit exists such that treatment of HF remains suboptimal for a significant number of patients.

Electronic Health Records

While clinical registries focus on populations, prospectively defining specific aims before data collection and analysis, EHRs focus on individual patients, collecting, sharing, and deploying personal health information for the benefit of the patient (Gliklich et al, 2014). In the US, most HCPs routinely use EHR platforms to document point-of-care interactions with their patients (Health IT Dashboard, 2018). Besides managing personal health information, EHRs also streamline patient and practice management, enhance quality of patient care, and support reimbursement of medical claims. EHR platforms are repositories for de-identified RWD from which RWE is derived (Jarow et al, 2017). These databases reflect how medical care is delivered in daily practice.
EHR systems may be interfaced with registries and other observational studies to advance the evidence base for effectiveness and safety of therapies as well as quality of care (Gliklich et al, 2014). When EHRs are rendered bi-directionally interoperable with registries, they enable efficient data capture and transformation, the latter perhaps through natural language processing, thereby yielding large quantities of diverse, readily available healthcare information for evidence development, while delivering information from the registry back to the clinician (Gliklich et al, 2014).

Motivated by the promise that health information technology could promote uniform adoption of recommended therapies for patients with systolic HF, investigators conducting an IMPROVE-HF registry that examined outpatient cardiology practices with no EHR, partial EHR, or fully implemented EHR systems reported that certain quality measures (i.e., use of ACEI or ARB, aldosterone antagonists, and HF patient education) but not others (i.e., use of beta blockers, anti-coagulants, cardio-resynchronization devices, and implantable cardioverter-defibrillators) were improved for patients at cardiology practices using partial and fully implemented EHR platforms (Walsh et al, 2010). In an observational study conducted in three hospitals with newly implemented EHR systems, improved endpoints (i.e., fewer tests, fewer medications, and improved survival) were demonstrated for patients with chronic congestive HF who presented to the EDs from within the EHR systems but not for patients who were external to the EHR systems in two of three hospitals (Connelly et al, 2011). A more recent study drawing on hospitals in the GWTG-HF registry with no, partial, or fully implemented EHR systems that examined quality metrics among patients hospitalized for HF found a positive association only for beta-blocker prescribing at discharge in hospitals with fully implemented EHR systems (Selvaraj et al, 2018). Taken together, these findings suggest implementation of EHR systems may enhance clinical decision support in the clinical workflow.

**REAL-WORLD CASE STUDY**

To explore how real-world observations might provide insight into managing systolic HF, an analysis was performed on de-identified RWD from ambulatory patients with HF using the Practice Fusion EHR platform, a Veradigm™ brand. Practice Fusion is the largest cloud-based EHR platform in the US (Practice Fusion, 2019a). The Practice Fusion EHR contains over 100 million patient records sourced from more than 6% of physicians in the US (Practice Fusion, 2019b; IQVIA, 2018). The platform enables secure, bi-directional communication between Practice Fusion and HCPs.

The objectives of this case study were to characterize ambulatory patients with systolic HF and to explore adoption of the two newest pharmacotherapies for patients with systolic HF, available in the US since the second half of 2015.

**Study Design**

This retrospective, observational study evaluated de-identified data (demographics, comorbidities, prescription medications, and provider specialty) from ambulatory patients who had a prescription for at least one of two pharmacotherapies, ARNI or IVB, compared with data from patients naïve to these treatments.
The study design is shown in Figure 1. Patients were stratified into two groups according to their exposure to GDMT medications in the 12-month Baseline period (i.e., with or without at least one written prescription for a GDMT medication [ARNI and IVB were excluded from GDMT at Baseline]). Patients were further stratified according to prescription for GDMT with or without ARNI and/or IVB (ARNI-IVB) from Index until the end of the study intake, for a total of four cohorts (i.e., No Baseline GDMT/Naive, No Baseline GDMT/ARNI-IVB, Baseline GDMT/Naïve, and Baseline GDMT/ARNI-IVB).

To be included in the study, patients had to:

- Have at least one prescription written for a medication recognized as GDMT (Yancy et al, 2017) (see Table 1) during study intake between January 1st and December 31st, 2018 (the Index date). Index dates were defined as follows:
  - Patients with ARNI-IVB during study intake: Index date is the earliest written prescription date for ARNI-IVB
  - Patients without ARNI-IVB during study intake: Index date is the earliest written prescription date for a GDMT medication
  - (All patients were required to be ARNI-IVB-Naïve prior to Index)
- Be 18 years of age or older at Index
- Have at least one ambulatory visit to an HCP more than 12 months prior to Index.
RESULTS

A total of 64,396 patients were identified who had at least one written prescription for a GDMT medication during the study intake period. From this initial pool of candidates, 45,948 patients additionally met age and prior HCP visit criteria. At Index, 14,079 (30.6%) patients had no prior written prescription for a GDMT medication, during the 12-month Baseline period (cohorts: No Baseline GDMT/Naïve and No Baseline GDMT/ARNI-IVB); 31,869 (69.4%) patients had at least one prior written prescription for a GDMT medication, during the Baseline period (cohorts: Baseline GDMT/Naïve and Baseline GDMT/ARNI-IVB).

Of the 45,948 patients who qualified, 1,536 (3.3%) had at least one written prescription for ARNI-IVB during study intake. The proportion of written prescriptions for ARNI IVB in this ambulatory population is similar to that reported (2.3%) in a GWTG-HF registry of patients who were prescribed ARNI at discharge during the first year after its launch (Luo et al, 2017) and to that reported (<3%) in a study that evaluated claims data for privately insured and Medicare Advantage beneficiaries who filled a first prescription for ARNI in the first 18 months following FDA approval (Sangaralingham et al, 2018). In an ongoing registry (CHAMP-HF), 15% of patients were prescribed ARNI; highest ARNI use was associated with larger clinical practices (DeVore et al, 2018).

### TABLE 1 | GDMT for Stage C Systolic Heart Failure

<table>
<thead>
<tr>
<th>Category</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldosterone receptor antagonists (mineralocorticoid antagonists) (MCAs)</td>
<td>Spironolactone or eplerenone</td>
</tr>
<tr>
<td>Angiotensin Converting Enzyme Inhibitors (ACEIs)</td>
<td>Captopril, enalapril, fosinopril, perindopril, lisinopril, quinapril, ramipril, or trandolapril</td>
</tr>
<tr>
<td>Angiotensin II Receptor Blockers (ARBs)</td>
<td>Candesartan, losartan, or valsartan</td>
</tr>
<tr>
<td>Angiotensin II Receptor/Nephrilysin Inhibitor (ARNI)*</td>
<td>Sacubitril/valsartan*</td>
</tr>
<tr>
<td>Beta-adrenergic receptor antagonists (β-Blockers)</td>
<td>Bisoprolol, carvedilol, carvedilol CR, or metoprolol succinate CR/XR</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Loop diuretics; furosemide, torsemide, or bumetanide Other potassium-sparing diuretics: amiloride or triamterene Thiazide diuretics: chlorothiazide, chlorthalidone, hydrochlorothiazide, indapamide, or metolazone</td>
</tr>
<tr>
<td>If Channel Blocker</td>
<td>Ivabradine (IVB)*</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Hydralazine-isosorbide dinitrate or hydrazaline/isosorbide nitrate</td>
</tr>
</tbody>
</table>

GDMT = guideline-directed medical therapy.  *ARNI and IVB were excluded from GDMT at Baseline.
Demographics

Patient demographics are shown in Table 2. The mean ages for the four cohorts ranged from 66.0 years to 70.8 years. There were differences in gender distribution between naïve (No Baseline GDMT/Naïve plus Baseline GDMT/Naïve) and ARNI-IVB (No Baseline GDMT/ARNI-IVB plus Baseline GDMT/ARNI-IVB) cohorts; in the naïve cohorts, there were approximately equal numbers of male and female patients whereas in the ARNI-IVB cohorts, more patients were male (61.5% & 66.0%), consistent with gender distributions reported in a registry of hospitalized patients with systolic HF (EF <40%) (Luo et al, 2017).

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Patient Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHARACTERISTICS</td>
<td>No Baseline GDMT/Naïve N=13,788</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>70.0 (12.9)</td>
</tr>
<tr>
<td>GENDER</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>47.5%</td>
</tr>
<tr>
<td>Male (%)</td>
<td>52.4%</td>
</tr>
<tr>
<td>Not Recorded</td>
<td>0.1%</td>
</tr>
<tr>
<td>RACE</td>
<td></td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>42.6%</td>
</tr>
<tr>
<td>African American (%)</td>
<td>13.2%</td>
</tr>
<tr>
<td>Other (%)</td>
<td>7.6%</td>
</tr>
<tr>
<td>Undocumented (%)</td>
<td>36.6%</td>
</tr>
<tr>
<td>ETHNICITY</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino (%)</td>
<td>20.1%</td>
</tr>
</tbody>
</table>

GDMT = guideline-directed medical therapy; SD = standard deviation; ARNI = angiotensin receptor-neprilysin inhibitor, sacubitril/valsartan; IVB = I f sinoatrial channel blocker, ivabradine.
The regional distribution of study-eligible patients, whether naïve to ARNI-IVB (n=44,412) or with written prescriptions for ARNI-IVB (n=1,536) is shown in Figure 2. The recorded regional distributions of patients in the naïve and ARNI-IVB cohorts were similar, except for the distributions in the Northeast ( naïve, 16.3% vs ARNI-IVB, 24.3%) and in the West ( naïve, 19.4% vs ARNI-IVB, 22.2%).

**Charlson Comorbidity Index**

Comorbidities were summarized using the Charlson Comorbidity Index (CCI), a well-established measure that serves as a prognostic indicator of morbidity (Charlson et al, 1987; Rashid et al, 2017). Across the four cohorts, most patients (63.9%, 64.6%, 71.3%, and 75.3%) had CCI scores of 2 or higher. CCI scores >2 were indicative of higher one-year mortality risk among patients 65 years of age or older in a study that evaluated mortality after a first hospitalization for acute HF (Formiga et al, 2018). Mean (SD) scores were 2.8 (2.3), 2.5 (1.9), 3.2 (2.4), and 3.0 (2.0) for patients with No Baseline GDMT/Naïve, No Baseline/ARNI-IVB, Baseline GDMT/Naïve, and Baseline GDMT/ARNI IVB, respectively (Table 3). Among discrete non-cardiovascular comorbidities relevant to systolic HF were chronic pulmonary disease (range across all cohorts, 25.8%-32.1%), diabetes without chronic complications (range, 34.4%-44.3%), and renal disease (range, 19.9% 25.9%); each of these generally aligned with the findings of the CHAMP-HF registry of ambulatory patients with systolic HF (Greene et al, 2017).
TABLE 3 | Comorbidities

<table>
<thead>
<tr>
<th>CHARLSON COMORBIDITY INDEX (CCI)</th>
<th>No Baseline GDMT N=14,079</th>
<th>Baseline GDMT N=31,869</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Naïve</td>
<td>ARNI-IVB</td>
</tr>
<tr>
<td></td>
<td>n=13,788</td>
<td>n=291</td>
</tr>
<tr>
<td>CCI (mean [SD])</td>
<td>2.8 (2.3)</td>
<td>2.5 (1.9)</td>
</tr>
<tr>
<td>AIDS/HIV</td>
<td>22 (0.2%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Any malignancy</td>
<td>913 (6.6%)</td>
<td>23 (7.9%)</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>1,935 (14.0%)</td>
<td>31 (10.7%)</td>
</tr>
<tr>
<td>Chronic Pulmonary</td>
<td>3,824 (27.7%)</td>
<td>75 (25.8%)</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>8,760 (63.5%)</td>
<td>244 (83.8%)</td>
</tr>
<tr>
<td>Dementia</td>
<td>309 (2.2%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Diabetes with Chronic Complication</td>
<td>2,032 (14.7%)</td>
<td>21 (7.2%)</td>
</tr>
<tr>
<td>Diabetes w/o Chronic Complication</td>
<td>4,749 (34.4%)</td>
<td>106 (36.4%)</td>
</tr>
<tr>
<td>Hemiplegia or Paraplegia</td>
<td>210 (1.5%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>37 (0.3%)</td>
<td>3 (1.0%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>47 (0.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Metastatic Solid Tumor</td>
<td>48 (0.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Mild Liver Disease</td>
<td>708 (5.1%)</td>
<td>3 (1.0%)</td>
</tr>
<tr>
<td>Moderate or Severe Liver Disease</td>
<td>44 (0.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>1,069 (7.8%)</td>
<td>23 (7.9%)</td>
</tr>
<tr>
<td>Peptic Ulcer Disease</td>
<td>174 (1.3%)</td>
<td>3 (1.0%)</td>
</tr>
<tr>
<td>Peripheral Artery Disease</td>
<td>3,084 (22.4%)</td>
<td>35 (12.0%)</td>
</tr>
<tr>
<td>Renal Disease</td>
<td>2,983 (21.6%)</td>
<td>58 (19.9%)</td>
</tr>
<tr>
<td>Rheumatic Disease</td>
<td>569 (4.1%)</td>
<td>5 (1.7%)</td>
</tr>
</tbody>
</table>

GDMT = guideline-directed medical therapy; SD = standard deviation. ARNI = angiotensin receptor-neprilysin inhibitor, sacubitril/valsartan; IVB = I<sub>f</sub> sinoatrial channel blocker, ivabradine.
**Ambulatory Systolic HF Treatment**

*Figure 3* illustrates the percent distribution of patients with at least one written prescription for each class of GDMT medications comparing patients who were naïve to ARNI-IVB (Baseline GDMT/Naïve) to patients who had written prescriptions for ARNI-IVB (Baseline GDMT/ARNI-IVB), at Index or during the remainder of study intake. In the cohort naïve to ARNI-IVB, the percent of patients with written prescriptions was highest for diuretics (46.3%), followed by beta-blockers (42.4%), ACEIs (29.6%), ARBs (24.9%), aldosterone receptor antagonists (MRA, 9.8%) and vasodilators (7.1%). In the ARNI-IVB cohort, the percent of patients with written prescriptions was highest for ARNI (96.8%), followed by beta-blockers (50.4%), diuretics (47.2%), aldosterone receptor antagonists (MRA, 20.1%), vasodilators (4.9%), ivabradine 4.8%, ARBs (4.4%), and ACEIs (3.1%).

**F I G U R E 3** | Percent of Patients with GDMT Medications at Index and Follow Up

<table>
<thead>
<tr>
<th>Class</th>
<th>ARNI-IVB</th>
<th>NAÏVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>0.0%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Angiotensin-Converting Enzyme Inhibitors (ACEIs)</td>
<td>0.0%</td>
<td>29.6%</td>
</tr>
<tr>
<td>Angiotensin Receptor Blockers (ARBS)</td>
<td>4.4%</td>
<td>24.9%</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>50.4%</td>
<td></td>
</tr>
<tr>
<td>ARNI</td>
<td>96.8%</td>
<td></td>
</tr>
<tr>
<td>Mineralocorticoid Receptor Antagonists (MRAS)</td>
<td>20.1%</td>
<td></td>
</tr>
<tr>
<td>Vasodilators</td>
<td>4.9%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

*ARNI and IVB were excluded from GDMT at Baseline

Most (66.0%) ambulatory patients naïve to ARNI-IVB were managed by primary care practices. Over one-half (57.7%) of patients with prescriptions for ARNI-IVB were managed by practices with at least one cardiologist.
BNP and N-Term BNP

Between 3.1% and 13.8% of patients across the cohorts had lab values for BNP and NT-proBNP. For patients naïve to ARNI-IVB, the mean (SD) values for BNP and NT-proBNP were 404 (979) pg/ml and 1,764 (3,485) pg/ml, respectively. Corresponding values for patients with written prescriptions for ARNI IVB were 775 (1,711) pg/ml and 1,724 (2,268) pg/ml. NT-proBNP values are consistent with those reported for the 95th percentile of patients with chronic HF, NYHA functional Class II (University of Iowa, 2019).

DISCUSSION

Alleviating symptoms, reducing rates of hospitalization for acute exacerbations, and preventing premature death are the primary goals of HF therapy (McMurray, 2010). A multidisciplinary approach that focuses on care identification and coordination, management of comorbidities, individualization of therapy, and patient education is essential for its treatment (Bozkurt, 2018). For patients with systolic HF, substantial clinical evidence is available to guide treatment, with information on pharmacotherapies, devices, biomarkers, and diagnostic and care strategies continually being updated in treatment guidelines and consensus decision publications. Despite recent advances in therapeutic options, treatment of systolic HF remains suboptimal for a significant number of patients.

The case study provides an example of how ambulatory patient data (i.e., demographics, comorbidities, prescription medications, and provider characteristics) from an EHR platform may be leveraged to generate RWE. This retrospective case study, which used de-identified RWD from the EHR platform Practice Fusion, a Veradigm offering, demonstrates that prior to Index, nearly one third of these ambulatory HF patients were not receiving at least one GDMT. The case study and other studies (Luo et al, 2017; Sangaralingham et al, 2018; DeVore et al, 2018) suggest that new medications specifically approved for the treatment of systolic HF may be underutilized despite being important advances in HF patient care (Yancy et al, 2016).

The adoption of several classes of cardiovascular medications with proven efficacy has taken longer and has been at a rate lower than expected. Over an 11-year period, the use of warfarin (for atrial fibrillation), beta-blockers and low-dose aspirin (for coronary artery disease), and ACEIs (for congestive HF) was reported to increase slowly; for ACEIs, utilization increased from 24% in 1990 to 36% in 1996 but then appeared to plateau, rising only 3% over the next five years (Stafford and Radley, 2003). Likewise, investigators found that following a period of slow growth (1990-2003), some therapies (aldosterone receptor antagonists) reached a plateau, whereas others (ACEIs, ARBs, beta-blockers, digoxin, and diuretics) declined in usage, based on physician surveys conducted between 2004 and 2009 (Banerjee and Stafford, 2010).

The selection of patients in the case study was based in part on diagnosis codes encompassing possible or probable systolic HF. Evolving natural language processing (NLP) capability of EHR platforms may enable efficient capture and transformation of additional data that are not available in structured data fields but are highly relevant to systolic HF (e.g., echocardiographic results, ejection fraction and NYHA classification from unstructured physician notes).
Digital health information systems that are primary sources of de-identified patient data enable bi-directional communication between EHR platforms and HCPs. EHRs provide an opportunity for care coordination by collecting and integrating patient information and facilitating distribution among all authorized HCPs (HealthIT.gov, 2018). Large, cloud-based EHRs such as Practice Fusion not only contain patient information but also provide access to evidence-based tools; they have the potential to be used in automating and streamlining HCP workflow, enabling shared decision-making regarding patient care, and supporting key changes in response to payer requirements and consumer expectations (HealthIT.gov, 2018). Bi-directional EHR platforms may initiate periodic communication with HCPs, comparing their conformity with nationally endorsed programs, including GDMT, to foster care plans that are aimed at improving patient quality of life, reducing HF-related hospitalizations, and extending survival. Health plans may be notified regarding members at high risk for acute exacerbations, whether due to recent laboratory findings (e.g., rising serum levels of natriuretic peptides) or non-adherence with GDMT, and provide support to members, who may be offered participation in enhanced care management programs and encouraged to adopt significant lifestyle adjustments or to discuss ongoing treatment with their HCPs through initiatives that promote health and wellness literacy.

As observational studies, registries in HF have been used extensively for gaining insight into clinical presentation, patient care, and treatment outcomes as well as in identifying gaps in the use and dosing of evidence-based, guideline-recommended pharmacotherapies. Because EHRs collect comprehensive health information from all clinicians involved for the benefit of individual patients, they are ideally suited for interfacing with registries in surveilling for trends in safety and management as Fast Healthcare Interoperability Resources (FHIR) are implemented (Hay, 2018). EHRs may facilitate registries by assessing feasibility, by identifying HCPs with eligible patients, and by hosting case record forms for uniform data capture to achieve registry objectives (Thomson and Levy, 2013). Data exchanged between registries and EHRs may also be leveraged to inform coverage decisions for drugs and procedures and as input for system-wide or community-based HF programs. Given web-based deployment of its Practice Fusion EHR platform, commitment to interoperability standards, and management and dispersal of health information through systems certified as compliant with the Health Information Trust Alliance (HITRUST), Veradigm is working to support and enable registry and study implementation using de-identified data from its EHR platforms.

That RWE may supplement the findings of RCTs underlies its potential usefulness in identifying additional indications for drugs available in the marketplace or in supporting post-approval regulatory efforts. For example, following the approval of candidate pharmacotherapies, questions may arise that are related to dosing or to subpopulations not previously studied; these may not be readily addressed by conducting additional RCTs (Jarow et al, 2017). The use of RWE may inform drug development in a manner that is both timely and cost effective, with findings germane to patients from broader settings than clinical research (Sherman et al, 2016).

The applicability of real-world electronic data capture to drug development is not restricted to the generation of RWE. When combined with RCTs in drug development programs, RWD may contribute to efficiency increases and cost reductions; such use is acknowledged and encouraged by the FDA (Food and Drug Administration, 2018a). As examples, RWD may be used in hypothesis generation, in assessing study feasibility, in identifying baseline characteristics of patients for
purposes of enrichment or stratification, in establishing biomarkers and other tools, in providing a basis for power calculations, and in assembling patient groups across geographic locations (Jarow et al, 2017; US Food and Drug Administration, 2018a).

Currently, the FDA uses RWD and RWE primarily for regulatory decisions related to safety and allows their limited use in evaluations of efficacy (e.g., in establishing comparison arms in oncology or rare disease interventional trials having single-arm design). In support of new indications or other label revisions for approved drugs or to support post-approval study requirements, the FDA recognizes RWD and RWE may be more fully integrated into the regulatory decision-making process (US Food and Drug Administration, 2018c). To this end, the newly implemented Framework for the Real-World Evidence Program (US Food and Drug Administration, 2018a) is directed toward leveraging RWD and RWE to inform and enable FDA decisions on therapeutic development. The new framework will be used to guide the FDA and biopharma in evaluating how to best use RWE to further stated goals (US Food and Drug Administration, 2018c).

**CONCLUSION**

There is growing interest in how electronic health information platforms may facilitate healthcare decision-making and efficient, cost-effective drug development. The evolving use of RWE in evaluating and communicating healthcare metrics will be critical to advancing appropriate care plans in HF. The results of a retrospective case study using Veradigm’s Practice Fusion EHR demonstrates how RWE from patients with systolic HF aligns with previous real-world analyses of disease burden. Future studies that leverage RWE from multiple electronic platforms may provide insight into patient quality of life, hospitalizations, and survival in the HF population.
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Veradigm is an integrated data systems and services company that combines data-driven clinical insights with actionable tools for clinical workflow, research, analytics and media. Our solutions are designed to help key healthcare stakeholders to improve the quality, efficiency, and value of healthcare technology partners, and most importantly, the patients they serve.

We are dedicated to simplifying the complicated healthcare system with next-generation healthcare solutions. This is how we are transforming health, insightfully.