What Managed Care Needs to Know in the Evolving Treatment of Heart Failure: Novel Therapies for Improved Clinical and Economic Outcomes

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Learning Objectives:

1. Describe the recently published guideline updates for emerging therapies in heart failure (HF), including results from pivotal trials and evidence supporting averted HF-related hospitalizations and/or deaths.
2. Summerize the mechanisms of action and different clinical attributes, including efficacy and safety, of new and emerging therapies for the management of HF.
3. Evaluate methods for individualizing chronic HF treatment strategies for patients based on specific patient-related factors to control symptoms, reduce hospitalizations, and prevent mortality in patients with reduced ejection fraction.
4. Characterize the disease burden of HF in the managed care setting as determined by hospitalizations and other components of morbidity and mortality.
5. Discuss current economic and logistic barriers to appropriate HF therapy in the managed care setting.
6. Employ collaborative strategies for HF management enlisting the input and support of a multi-disciplinary team of health care providers.
7. Apply methods to enable optimal cost management of newer HF therapy to be realized by multiple HF stakeholders including managed care organizations.
8. Apply evidence-based and expert consensus strategies for patient-centered HF care, including patient/caregiver education, shared decision-making, self-care and self-monitoring, and adherence promotion.

Faculty Disclosure:
Dr. Desai has received grants for clinical research from Novartis Pharmaceuticals Corporation and serves as a consultant for Abbott, AstraZeneca, DalCor Pharma, Novartis Pharmaceuticals Corporation, and Relypsa.
Dr. Dunlap has no relevant financial relationships to disclose.
Ms. Mack has no relevant financial relationships to disclose.
Dr. Owens has served on an advisory board or panel for Novartis Pharmaceuticals Corporation.

All material has been peer reviewed for bias.

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Post-Test Questions

1. Which of the following is NOT a risk factor for heart failure?

   a. Coronary heart disease b. Hypertension
   c. Overweight/obesity d. Asthma

2. Which of the following accounts for approximately 50% of direct heart failure?

   a. Medications b. Provider visits
   c. Hospitalizations d. Emergency room visits

3. Which of the following is the best choice for combining with neprilysin inhibitor for Renin-Angiotensin-Aldosterone (RAAS)inhibition while minimizing risk of angioendema?

   a. Angiotensin converting enzyme inhibitor (ACE-I)
   b. Angiotensin receptor blocker (ARB)
   c. Aldosterone antagonist
   d. Beta blocker

4. Which of the following is NOT an accurate statement about sacubitril/valsartan (angiotensin receptor blocker/neprilysin inhibitor, ARNI) treatment compared to enalaprin?

   a. ARNI reduced risk of cardiovascular death or heart failure hospitalization compared to enalaprin.
   b. Treatment with enalaprin improved quality of life compared to sacubitril/valsartan.
   c. Risk of Hypotension is greater with the combination than with enalaprin alone.
   d. Treating heart failure with sacubitril/valsartan provides an estimate one to two year increase in life expectancy over enalaprin use.

5. Which of the following is NOT a recommended regimen in the ACC/AHA guidelines for patients with chronic heart failure with reduced ejection fraction (HfrEF) to reduce morbidity and mortality?

   a. ARB + beta blocker + digoxin.
   b. ACE-I + beta blocker + mineralocorticoid receptor antagonist (MRA), (where appropriate).
   c. ARNI + beta blockers + MRA (where appropriate)
   d. ARB + beta blocker + MRA (where appropriate)

6. The guidelines recommend substituting ARNI for ACE-I or ARB in patients with chronic, symptomatic HfrEF NYHA Class II or III who tolerate and ACE inhibitor or ARB to further reduce morbidity and mortality.

   a. True b. False

7. Which of the following is a FALSE statement about Ivabradine?

   a. It is a selective I, inhibitor.
   b. There is no effect on myocardial contractility or relaxation like there is with beta blockers.
   c. There is a use-dependent block which means there is a low risk of bradycardia.
   d. This medication is also effective for atrial fibrillation.

8. Which of the following should be the target heart-rate with ivabradine therapy?

   a. < 80 bpm b. < 70 bpm
   c. < 60 bpm d. < 30 bpm

9. The primary place in therapy of ivabradine is to replace beta blockers in the recommended regimen for heart failure.

   a. True b. False

10. Which of the following is an evidence-based intervention to reduce readmission in heart failure?

    a. Pre-discharge HF education by trained educators
    b. Home visits by registered nurses and/or physicians
    c. Early post-discharge follow-up with provider
    d. All of the above

Activity Evaluation and Improvement Process

(Please rate this activity on the following scale:
4 - Excellent 3 - Good 2 - Fair 1 - Poor)

1. Based on the content presented, I am better able to:

   Describe the recently published guideline updates for emerging therapies in heart failure (HF), including results from pivotal trials and evidence supporting averted HF-related hospitalizations and/or deaths.

   4 3 2 1

   Summerize the mechanisms of action and different clinical attributes, including efficacy and safety, of new and emerging therapies for the management of HF.

   4 3 2 1

   Evaluate methods for individualizing chronic HF treatment strategies for patients based on specific patient-related factors to control symptoms, reduce hospitalizations, and prevent mortality in patients with reduced ejection fraction.

   4 3 2 1

   Characterize the disease burden of HF in the managed care setting as determined by hospitalizations and other components of morbidity and mortality.

   4 3 2 1

   Discuss current economic and logistic barriers to appropriate HF therapy in the managed care setting.

   4 3 2 1

   Employ collaborative strategies for HF management enlisting the input and support of a multi-disciplinary team of health care providers.

   4 3 2 1

   Apply methods to enable optimal cost management of newer HF therapy to be realized by multiple HF stakeholders including managed care organizations.

   4 3 2 1

   Apply evidence-based and expert consensus strategies for patient-centered HF care, including patient/caregiver education, shared decision-making, self-care and self-monitoring, and adherence promotion.

   4 3 2 1

2. The activity and presenters were free of bias.

   4 3 2 1

3. The activity was applicable to my position.

   4 3 2 1

4. How confident are you in managing patients based on this activity? (4 very confident - 1 not confident)

   4 3 2 1

5. Do you plan to change management strategies or patient care in your organization or practice based on the content presented?

   ☐ Yes ☐ No

6. If yes, what changes do you plan to implement in management strategies or patient care in your organization or practice?

   _____

   _____

   _____

7. Did the content of the activity help in meeting your above goal?

   ☐ Yes ☐ No

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Heart Failure Monograph 2018

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What Managed Care Needs to Know in the Evolving Treatment of Heart Failure: Novel Therapies for Improved Clinical and Economic Outcomes

Akshay S. Desai, MD, MPH; Mark E. Dunlap, MD; Sharon Mack, APRN-CNP; Gary Owens, MD

Introduction

HEART FAILURE (HF) IS A COMPLEX CLINical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood.[1] Risk factors for HF include coronary heart disease, hypertension, diabetes, overweight/obesity, and unhealthy behaviors (smoking; eating foods high in fat, cholesterol and sodium; physical inactivity).

Heart failure (HF) is a major public health problem, with prevalence of more than 5.8 million in the United States (U.S.), and over 23 million worldwide.[2] Approximately 960,000 new cases are diagnosed annually. As our population continues to age, the prevalence of HF will increase by an estimated 25 percent by 2030.[3] About half of the people who develop HF die within five years of diagnosis; this is a much worse five-year survival rate than many cancers. Given the improvements in therapy which are impacting mortality, HF is the only major CV disease increasing in incidence and prevalence.

HF is an expensive disease to manage and these costs will only increase as the prevalence increases.[3] Direct costs may range from $60.2 billion to $115.4 billion, when HF is considered either in isolation or as part of a syndrome.[4] The 2030 projected cost estimates of treating just HF are $160 billion.[3] Yearly, direct costs are estimated at $20,245 per patient. Prescription costs range from $750 to $1,626 per person per year. Emergency department costs are over $500 million per year. Indirect costs are estimated at $10.6 billion.[4]

Hospitalizations account for about 50 percent of direct costs of HF; there are very high rates of hospitalizations and readmissions with this disease. The majority of hospitalizations are in those with worsening chronic HF, as compared to those with de novo HF or refractory HF.[5] HF is the condition responsible for the most hospital readmissions; the cost of HF readmissions for all Medicare patients each year is $26 billion.[5] Total lifetime direct costs of care are estimated to be over $100,000 per person, with 77 percent of that cost being attributed to hospitalization.[6]

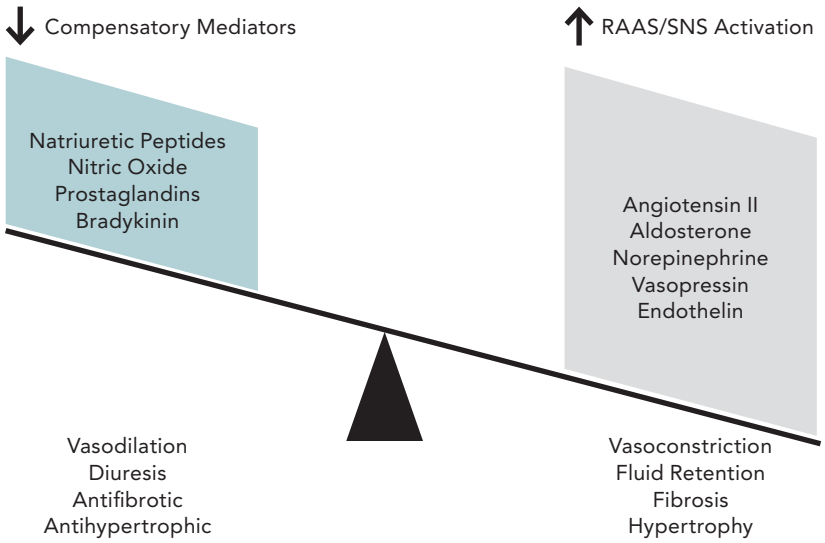
Hospital readmissions for HF are a serious issue for patients, providers, health care systems, and payers. Twenty percent or more of patients are readmitted within 30 days and 50 percent within six months.[7,8] Despite attempts to lower readmissions, these rates have remained largely unchanged since the start of the new millennium. Predicting which patients will be re-hospitalized is difficult and much is unexplained. More than one-half of health systems are paying penalties for readmissions. Medicare fee-for-service patients at hospitals subject to penalties had greater reductions in readmission rates compared with those at non-penalized hospitals.[9] This will continue to be an area of payer cost burden and payer focus.

Treatment

HF can be thought of as a consequence of initially compensatory neurohormonal mechanisms which become maladaptive. The key systems that are activated are the renin angiotensin and aldosterone system (RAAS) and the sympathetic nervous system (SNS, Exhibit 1). Treatment of HF seeks to interrupt the effects of these neurohormonal mechanisms. The majority of treatments have worked on the RAAS/SNS side of the equation, but therapies are now available that enhance the compensatory mediators (neprilysin inhibitors).

In the ACCF/AHA 2013 guidelines, the last full guideline publication, a step approach was used starting with loop diuretics supplemented with thiazides, if needed, for fluid overload to which an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) and then beta-blockers were added to slow the progression of the disease and improve mortality.[10] Therapy was guided primarily by NYHA functional class. There is a large amount of consensus data that those with

Exhibit 1: Neurohormonal Balance in Heart Failure



an ejection fraction (EF) less than 40 percent, even if asymptomatic, should be getting the combination of an ACE-I/ARB and a beta-blocker, which are titrated to target doses. If symptoms are not controlled by the combination of ACE /ARB and beta-blocker, a mineralocorticoid receptor agonist (spironolactone or eplerenone) was added. Other therapies which could be used are hydralazine/isosorbide dinitrate and or digoxin. These last two therapy options are primarily for patients who cannot tolerate the primary therapies or whom still have symptoms on a maximized regimen of the preferred agents.

It is important to try to achieve target dosing with ACEIs/ARBs and beta-blockers. Even though blocking angiotensin II is a key step in preventing progression, there do appear to be diminishing returns in blocking the RAAS system. The combination of an ACE-I and an ARB has been shown to reduce hospitalization, but it does not improve mortality. The combination also increases the risk of hyperkalemia and worsening renal function.

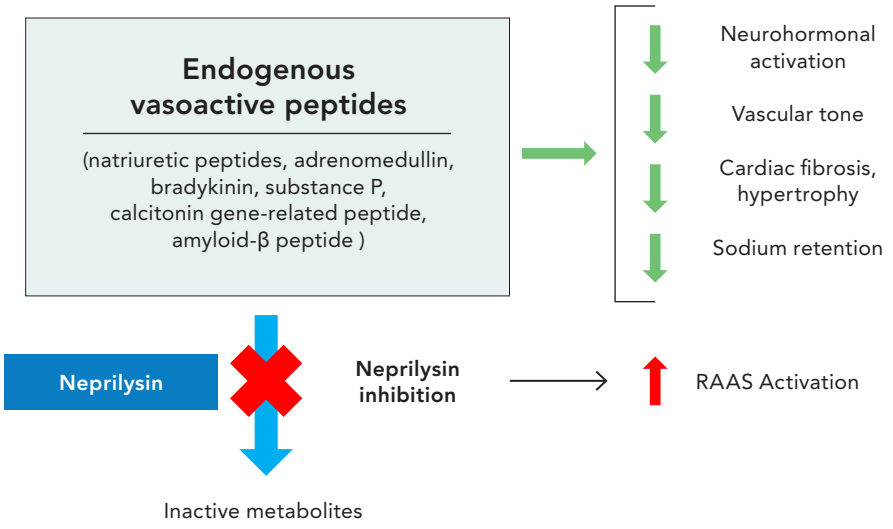
Neprilysin Inhibitors

One new therapy for HF uses neprilysin inhibitors, which has led to changes in the management guidelines. Neprilysin is important in the breakdown of various endogenous vasoactive peptides (Exhibit 2). Blocking its action enhances the circulating levels of these peptides and their effects. Higher levels of the vasoactive peptides can blunt the effects of the RAAS/SNS. Unfortunately, some things like angiotensin II are also substrates for neprilysin; neprilysin inhibitors also increase angiotensin II levels, which are counterproductive in HF. Thus, neprilysin inhibitors cannot be used alone in HF and must be combined with RAAS inhibition.

The combination of a neprilysin inhibitor and an ACE-I results in a very high rate of angioedema. This is thought to occur because of inhibition of three key pathways for bradykinin breakdown. Combination with an ARB leaves the pathways for bradykinin breakdown intact and thus lower risk of angioedema. Sacubitril was the first marketed neprilysin inhibitor, and it is marketed in a combination formulation with valsartan (Entresto®) and referred to as an angiotensin receptor neprilysin inhibitor (ARNI).

In the Paradigm-HF trial, sacubitril/valsartan, compared with enalapril, resulted in a 4.7 percent absolute risk reduction in the combined endpoint of cardiovascular (CV) death or HF hospitalization (Exhibit 3).[11] In this trial, subjects got the best available therapy at the time; 90 percent were on a beta-blocker and about 50 percent were on a mineralocorticoid receptor antagonist. The number-needed-to-treat with the combination is 21 to prevent one event. The other key endpoints of this trial are shown in Exhibit 4.[11,12] About 15 percent of subjects in the trial were treated with an implantable cardioverter defibrillator (ICD); the magnitude of treatment benefit of sacubitril/valsartan in terms of HF and sudden death was consistent in patients with and without an ICD. The other message of this trial was

Exhibit 2: Neprilysin as a Therapeutic Target in Heart Failure



the residual risk in a well-treated HF population. At one year, there was still a 15 percent risk of CV death or HF hospitalization in the enalapril group and 7 percent in the sacubitril/valsartan group. Using this new combination is an opportunity for improvement in medical therapy and reduction in residual risk. Overall, treating HF with sacubitril/valsartan provides an estimated one to two-year increase in life expectancy over enalapril use.[13]

There was also a quality of life analysis in this trial. Patients felt better in terms of symptoms, physical limitations, and social interactions and had better overall quality of life in the sacubitril/valsartan group compared to the enalapril treated group.[14]

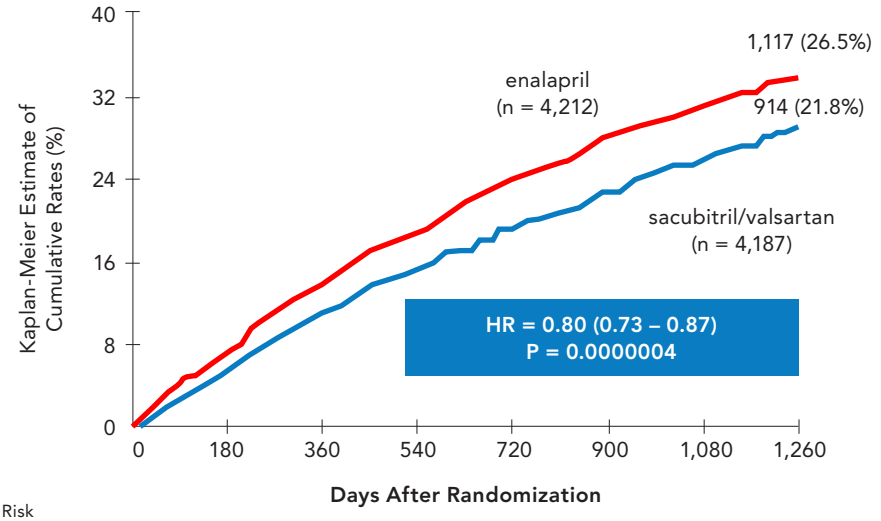
Fewer sacubitril/valsartan-treated patients experienced worsening HF symptoms or required intensification of medical treatment, emergency department evaluation, intensive care, or inotropic support for HF than those treated with enalapril. The time to the first HF hospitalization was increased, and the cumulative HF hospitalization rates were decreased with the combination.[15] Both all-cause and HF-related 30 and 60-day hospitalization readmissions were decreased by the combination (Exhibit 5).[16]

The Paradigm-HF trial was one of the largest HF trials ever, and the endpoints were not surrogate markers. Some criticisms of this trial have been brought forward. Maximum doses of enalapril were not used in the comparator arm, the entry criteria were too restrictive (20 percent of screened patients were excluded), and the early termination due to improved mortality could have missed attenuation of effect over time.

There are some safety issues with this combination which need to be addressed. Risk of hypotension is greater with the combination than with enalapril alone (14% vs 9.2%). This is not unexpected given that sacubitril is a potent vasodilator. Angioedema is also a concern, especially in African Americans. To reduce the risk of angioedema, there should be a 36-hour gap between discontinuation of an ACE-I and initiation of sacubitril/valsartan. Hyperkalemia, cough, and renal impairment seem to occur less frequently with the combination than with an ACE-I alone. Sacubitril has to be initiated carefully and lower initial doses are recommended in selected populations [on low-dose ACE-I/ARB or ACE-I/ARB naïve, renal impairment (eGFR <= 30 mL/min/m^2), moderate Hepatic Impairment (Child-Pugh Class B), or elderly]. The dose is doubled every two to four weeks until the target dose of 97/103 mg twice daily is reached.

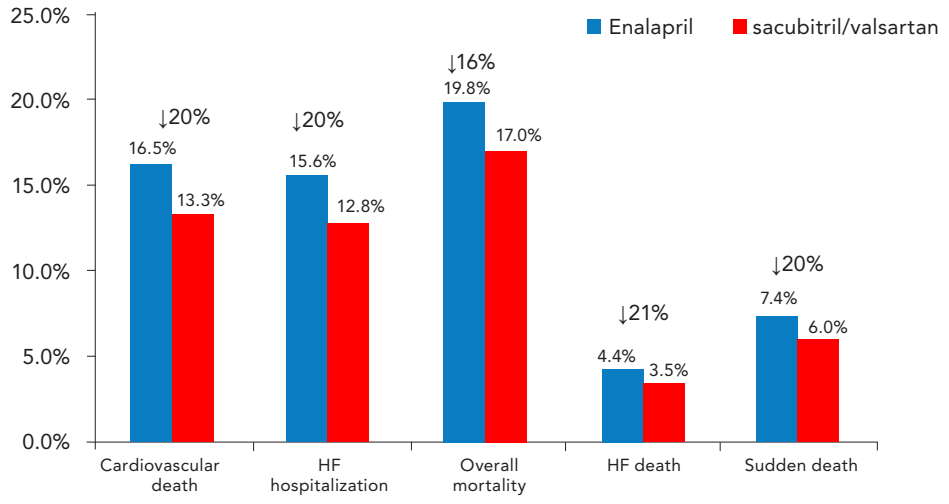
A cost-effectiveness analysis of sacubitril/valsartan has been done. A two-state Markov model of U.S. adult patients (mean age, 63.8 years) calculated that there would be 220 fewer hospital admissions per 1,000 patients with HF treated with sacubitril/valsartan versus enalapril over 30 years.[17] The incremental costs and quality-adjusted life-years (QALYs) gained with sacubitril/valsartan treatment were estimated at $35,512 and 0.78, respectively, compared with enalapril, equating to an incremental cost-effectiveness ratio (ICER) of $45,017 per QALY for the base-case. Sensitivity analyses demonstrated ICERs ranging from $35,357 to $75,301 per QALY.[17] This is a "high

Exhibit 3: PARADIGM-HF Primary Endpoint: CV Death or HF Hospitalization[11]



Patients at Risk								
sacubitril/valsartan	4,187	3,922	3,663	3,018	2,257	1,544	896	249
Enalapril	4,212	3,883	3,579	2,922	2,123	1,488	853	236

Exhibit 4: Other Key Endpoints of Paradigm-HF[11,12]

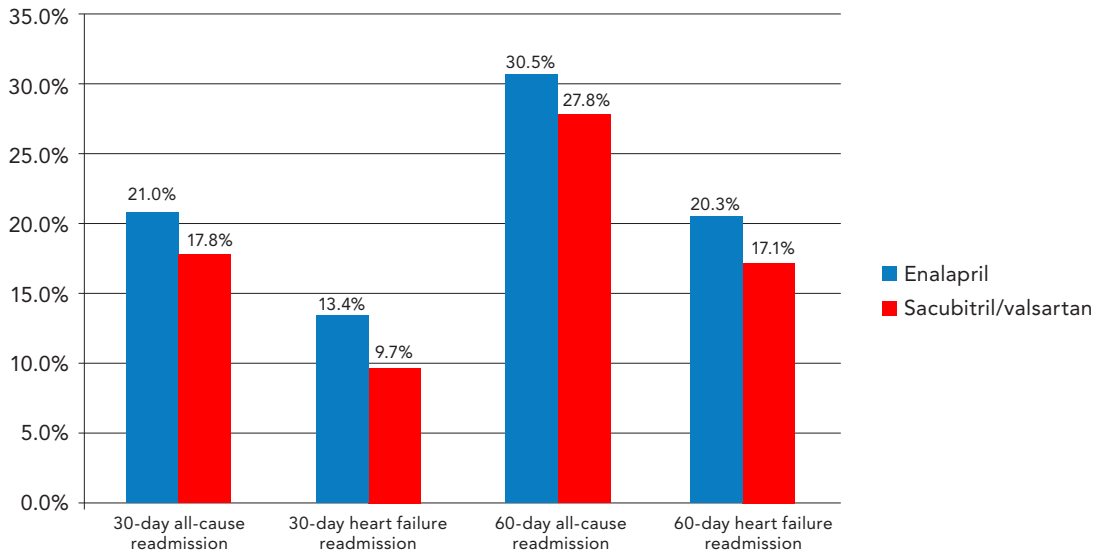


value"or "highly cost-effective" ICER by ACC/AHA and WHO metrics.

Guideline Updates for ARNI

The HF management guidelines have been updated to include ARNI (Exhibit 6).[18] An ACE-I or ARB or ARNI in conjunction with beta-blockers + MRA (where appropriate) is recommended for patients with chronic heart failure with reduced ejection fraction (HFrEF) to reduce morbidity and mortality. Furthermore, in patients with chronic, symptomatic HFrEF NYHA Class II or III, who

Exhibit 5: Effect of Sacubitril/Valsartan on Hospital Readmissions[16]



tolerate an ACE-I or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality. This patient population is that of the Paradigm-HF study.

Uptake of ARNI

Despite the benefits and recommendation for use, there has been a slow uptake of ARNI utilization.[19] Some of this early on was due to insurance barriers, and now the issue appears to primarily be dissemination of the information about benefit to community physicians. Another barrier has been clinicians thinking their patients are stable and not wanting to interfere with success. Apparent stability is not a good marker of which patient would benefit from ARNI use. In the Paradigm-HF trial, 20 percent of patients who had never been hospitalized for HF had a primary event during the study, and 17 percent died.[20] Of stable patients who experienced a primary event, death preceded heart failure hospitalization in 51 percent, with 60 percent of these deaths being sudden cardiac deaths. The opportunity to substitute ARNI for ACE-I or ARB may be lost if clinicians wait until the patient has worsening symptoms or hospitalization for HF.

When to Initiate ARNI

ARNI should be considered in NYHA II-III subjects tolerating ACE/ARB. They are a possibility for those on low dose ACE/ARB and ACE/ARB naïve patients. This group was not studied in the Paradigm-HF trial; tolerability may be an issue so lower doses should be started. It is unknown if ARNI will benefit Stage D HF, acutely hospitalized HF patients, and those with preserved EF. There is a large ongoing trial of ARNI in HF with preserved EF (HFpEF).

Ivabradine

The other new class of agents for HF target heart rate. Heart rate is an important target in HF treatment because elevated heart rate is an important contributor to disease progression (Exhibit 7). One benefit of beta-blockers is heart rate reduction; they also impact vasomotor tone, SNS activation, and remodeling. In HF, reducing heart rate improves outcomes, and therapies that increase heart rate worsen outcomes.[21,22]

The sinus node action potential generates the heart rate. This action potential is heavily driven by the I_f current. Ivabradine (Corlanor®) is a selective I_f inhibitor. I_f inhibition reduces the diastolic depolarization slope, thereby lowering heart rate. There is no effect on myocardial contractility or relaxation like there is with beta-blockers. At higher heart rates, ivabradine binds more efficiently, thus there is a use-dependent block, which means there is a low risk of bradycardia. This medication causes a selective reduction of heart rate in sinus rhythm; it is not effective in atrial fibrillation.

In the SHIFT trial, ivabradine was studied against placebo in 6,558 patients with NYHA II-

Exhibit 6: 2017 ACC/AHA/HFSA Guideline Update[18]

COR	LOE	Recommendations
I	B-R	ACEi OR ARB OR ARNI in conjunction with beta-blockers + MRA (where appropriate) is recommended for patients with chronic HFrEF to reduce morbidity and mortality.
I	B-R	In patients with chronic, symptomatic HFrEF NYHA class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.
III	B-R	ARNI should NOT be administered concomitantly with ACEi or within 36 hours of last ACEi dose.
III	C = EO	ARNI should NOT be administered to patients with a history of angioedema.
IIa	B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III), stable, chronic HFrEF (LVEF<=35%) who are receiving GDMT, including a beta-blocker at maximally tolerated dose, and who are in sinus rhythm with a HR>=70 bpm at rest.

IV HF, LVEF≤35 percent, prior HF hospitalization (within 12 months), and HR greater than 70 bpm in sinus rhythm on guideline-directed medical therapy (including beta-blocker at the maximum tolerated dose).[23] Seventy percent of patients in the trial achieved the target dose of 7.5 mg bid. This agent significantly reduced HR and the primary endpoint of reduced CV death and hospital admission for worsening HF by 18 percent. The effect was principally on HF hospitalization; there was a positive but not statistically significant benefit on HF death. Criticisms of this trial were shortfalls in the background medical therapy of the participants, and the majority of the patients in this study were not only from outside the U.S. but were also from outside Western Europe. The outcomes with ivabradine do appear to be better in those with higher heart rates at baseline (≥77), and reducing HR to less than 60 bpm provides the best outcomes with this medication.[24]

Safety issues include the potential for bradycardia, atrial fibrillation, phosphenes (seeing bright lights), and blurry vision. The I_f current is expressed in the retinal photo receptors, which contributes to phosphenes and blurry vision.

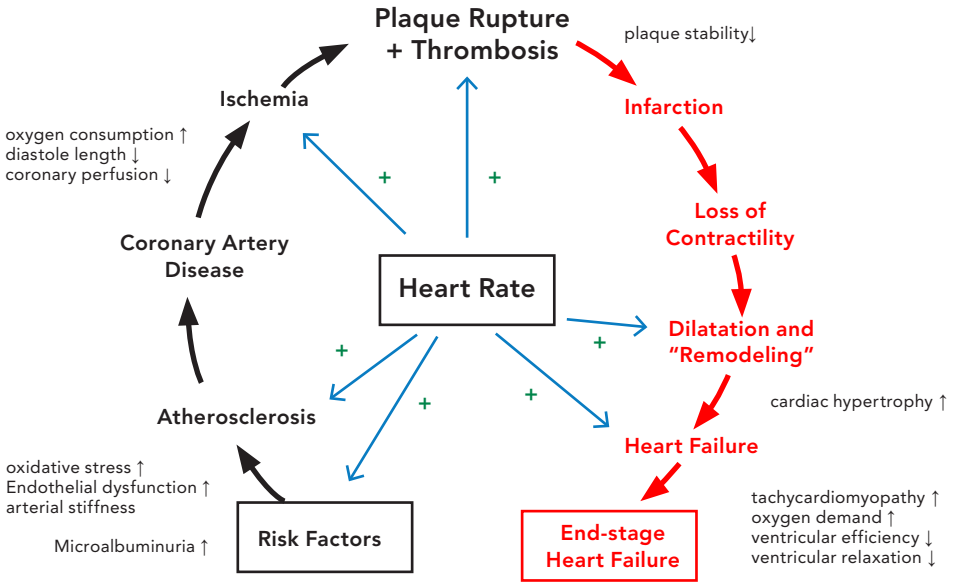
A cost-effectiveness analysis found that for a commercial population, the addition of ivabradine to background therapy was associated with cost savings and improved clinical outcomes.[25] For a Medicare Advantage population, the analysis indicated that the clinical benefit of ivabradine can be achieved at a reasonable cost (ICER- $24,920/QALY).[25]

The HF management guidelines recommend titrating beta blockers to maximal tolerated doses before adding ivabradine to achieve target HR (< 60 bpm) in appropriate patients (Exhibit 6).[18] The magnitude of HR reduction achieved with ivabradine and beta-blockade is the principal determinant of subsequent outcomes. The place in therapy for ivabradine is as a supplement to beta-blockers, and they may be especially useful in patients who do not tolerate target doses of beta-blockers. Overall, ivabradine is a new direction for the treatment of heart failure characterized by an elevated heart rate as a therapeutic target.

Improving Outcomes in HF

There are many different strategies for improving outcomes in HF, including ensuring clinician adherence with guideline-directed medical therapy (GDMT), targeting hospitalizations, caring for patients within a HF specialty practice, and targeting transitions in care.

Exhibit 7: Heart Rate and Cardiovascular Disease Progression



GDMT Adherence

The expert consensus pathway from the American College of Cardiology/American Heart Association (ACC/AHA) illustrates the practical application of GDMT in HF (Exhibit 8).[18,26] There are a large number of treatment options and opportunities to individualize therapy based on patient factors, but there is still plenty of room to improve outcomes in HF by making sure GDMT therapy is actually instituted and that it is done so at target doses. Exhibit 9 shows the rate of use of selected therapies from a large registry of outpatient cardiology practices.[27] Striking is the low rate of use of aldosterone antagonists in eligible patients; increased use of this class is encouraged by the guidelines.[18] This graphic likely underestimates the appropriate use because achievement of target dosing is not included. This analysis also only examined prescription of a class and not actual receipt. In another analysis, only 28 percent of patients received an adequate supply of ACE-I/ARB and beta-blocker in the 90 days before an ICD implantation.[28] Even the best medications do not work if the patient does not receive them or take them.

Reducing Hospitalizations

Much of the focus in improving outcomes has been on reducing hospitalizations and hospital readmissions within 30 or 60 days. Repeat hospitalizations for HF is a predictor of mortality.[29] Whereas clinicians used to think of a HF hospitalizations as an expense or inconvenience, it is now known that hospitalizations change the course of the disease and impact mortality. Thus, they are important to prevent.

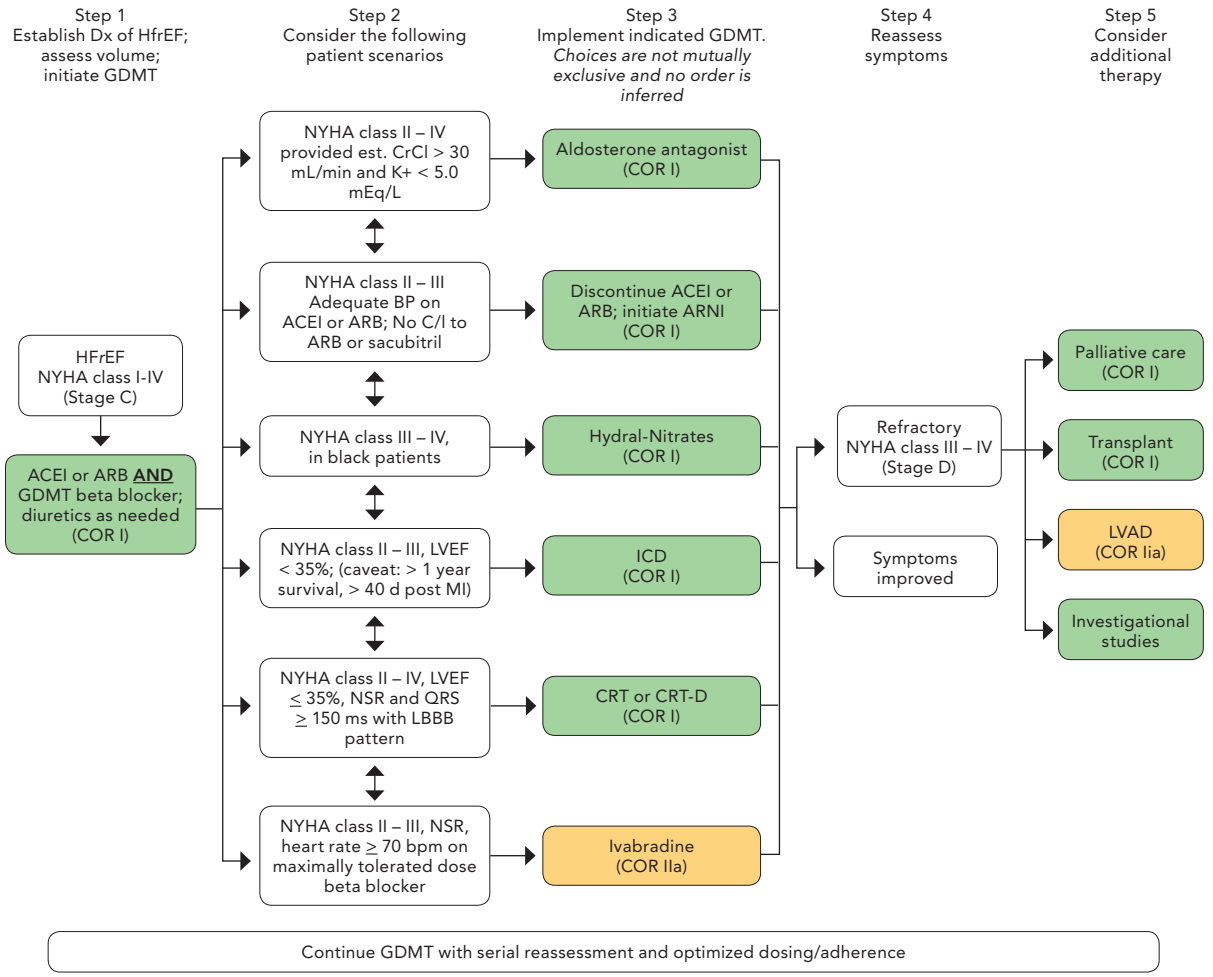
Evidence-based interventions to reduce readmission in HF include pre-discharge HF education by trained educators, discharge medication programs, comprehensive discharge planning, home visits by registered nurses and/or physicians, comprehensive HF disease management programs, implantable hemodynamic sensors, and early post-discharge provider follow-up (7-10 days).[10] It is clear that multiple interventions are needed to significantly reduce readmission rates.[30]

MetroHealth System achieved a 44 percent reduction in 30-day readmissions for HF between 2009 and 2016 (Exhibit 10). This significant reduction was the result of instituting numerous interventions (Exhibit 11). MetroHealth System has a dedicated HF discharge clinic and has added additional staff to accomplish all the interventions. They have visits where the patients only see a nurse in clinic, just for check in. In the MetroHealth System, all patients with HFrEF are required to have some level of contact with the HF team.

Heart Failure Specialty Care

Some data show that dedicated HF teams are better at managing HF than non-HF specialist cardiologists or primary care providers in terms of prescribing and achieving higher rates of target dosing for evidence-based therapy.[31,32] Dedicated HF teams also achieve lower readmission rates.[7,33]

Exhibit 8: Treatment of HFrEF Stage C and D[18,26]



Transition of Care

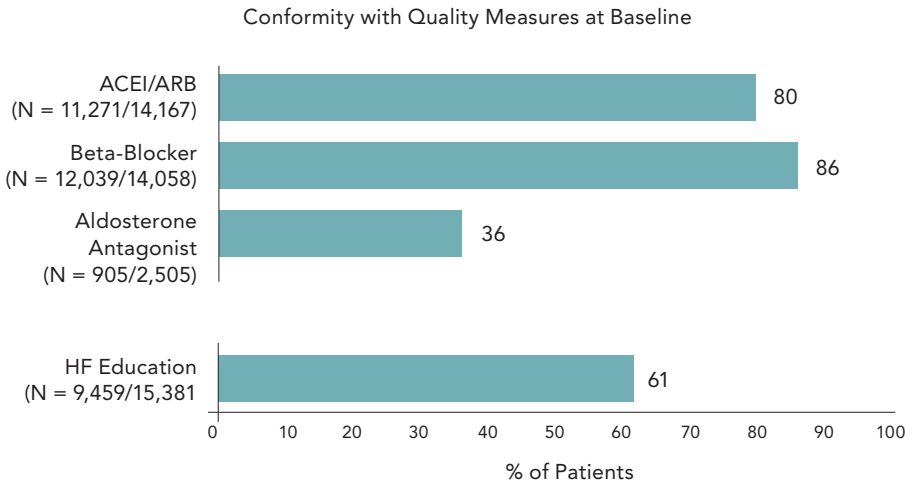
During transitions in care from hospital to home, or hospital to nursing home, or to other skilled nursing facilities, there are times where errors in GDMT prescribing and adherence can occur, resulting in readmission. Transitional care checklists can also be used to identify those at risk for readmissions. One such checklist, the Transitional Care Model, includes age 80 or older, moderate to severe functional deficits, an active behavioral and/or psychiatric health issue, four or more active co-existing health conditions, six or more prescribed medications, two or more hospitalizations within the past six months, a hospitalization within the past 30 days, an inadequate support system, low health literacy, and documented history of nonadherence to the therapeutic regimen.[34]

At times of transition from hospital to home, patients need a great deal of support. One program uses an advanced practice nurse coach to visit the patient in the hospital and at home 48 to 72 hours after discharge.[35] The coach also phones the patient three times during the coaching series. Each session emphasizes medication self-management, a patient-centered record owned and maintained by the patient, early follow-up (PCP or specialist), knowledge of red flags, and knowledge/skill of how to respond. The patient is instructed to keep a personal health record, which includes a problem list, medications, allergies, advance directives, warning symptoms, who to call, and patient questions. Use of this program results in significant reductions in 30 and 90-day readmissions.

Patient Education

Patient education is important in improving outcomes in HF, especially adherence with dietary changes, medications, and weight monitoring. Those providing patient education need to consider the Adult Learning Theory. Adults need to know why they are learning something and how it effects them directly. Lifetime experiences provide a basis

Exhibit 9: Utilization of GDMT in Practice: IMPROVE HF[27]



for learning and should be tapped as a resource for ongoing learning. For example, helping the patient remember how they felt when they had to be admitted to the hospital for HF. A hands-on problem solving approach to learning should be used, rather than a content-oriented approach. Adults need to apply new knowledge and skills immediately.

Another consideration for effective teaching and enhanced learning is health literacy. It is the newest vital sign and is the degree to which individuals obtain, process and understand basic health information and make appropriate health care decisions. A person who is health literate understands available health information (such as a diagnosis), uses this information to make good decisions about their care, chooses among treatment options, and knows how to use the health care system. Thirty-nine percent of HF patients have low health literacy.[36]

Low health literacy is a major barrier to learning about illness. The consequences of low health literacy include decreased health knowledge, poor self-management skills, decreased use of preventive services, poor medication adherence or difficulty in identifying their own medications, decreased ability to complete activities of daily living, decreased physical and mental health, increased hospitalizations and use of emergency services, and increased health care costs.[37-40] The increase in health care costs related to low health literacy is estimated at $73 billion per year.

Good communication techniques are always important, and they are critical when working with patients with low health literacy. Verbal techniques include slowing down, using common language and fewer medical terms, using pictures, using analogies or stories to personalize the message, and limiting information given in each interaction. Other verbal techniques include repeating information, focusing on key messages, presenting the most important points first, providing information in manageable chunks, and using active voice. Family, caregivers, and friends can be utilized to enhance learning. Ideally, written patient education materials should use one or two syllable words, four to six word sentences, and two to three sentence paragraphs to help those with low literacy. Written materials should not include medical jargon. The layout should have headings and bullet points, lots of white space, and key information should be highlighted, circled, or starred. Unfortunately, most written materials do not follow these guidelines. The readability of written materials can be assessed with various tools and so can a patient's literacy.

The Teach-back method is one effective way of providing patient education. The provider asks the individual to explain in his or her own words what was understood. It does not ask them if they understand. The provider then clarifies and reinforces the explanation as needed. This method reveals how well the provider explained a concept. Responsibility lies with the provider and that should be made clear to the patient. For example, the provider can say "I want to make sure I explained everything clearly to you. Can you please explain it back to me in your own words?" The Teach-back method is used after teaching each segment of information, such as sodium restriction. If a patient is not able to

Exhibit 10: HF 30 Day Readmissions: MetroHealth System vs. National Cohort

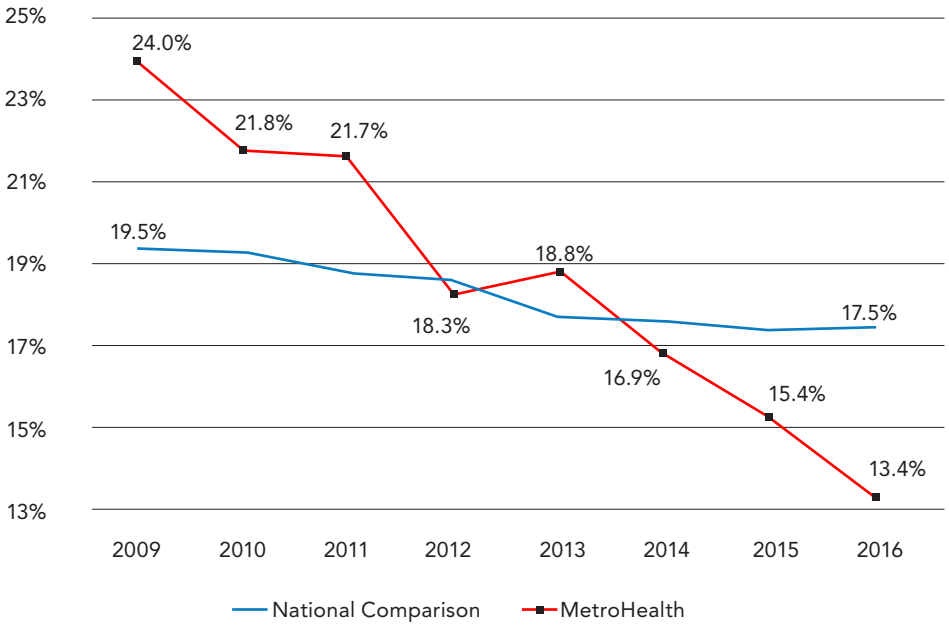


Exhibit 11: Efforts to Reduce HF Hospitalizations at MetroHealth System

1. Build staff (MDs, NP, PharmD, RNs, MTA, support staff)
2. Increase number of HF clinic visits
3. HF post-d/c clinic
4. RN visits
5. Phone calls (MD, NP, PharmD, RN)
6. Take care of higher acuity patients as options
7. Aggressive up-titration of HF meds
8. Med review/reconciliation
9. "Pharm-Assist" pharmacy clinics
10. HF specific transitional care coordinators
11. Case Managers (Internal Medicine and Family Practise)
12. Institute collaborative care across Departments and Services
13. HF Clinics deployed at many locations
14. CardioMems
15. Population Health Initiatives
16. Give to selected patients:
    a. Pill boxes
    b. HF medication bags
    c. HF education booklet
    d. Scales (limited, through grants)
17. Coordinate with home health
    a. VNA
    b. Ideal Home Health
    c. Red Carpet Care
18. Case Managers from third party payers (eg., Anthem BC/BS)
19. Inter-disciplinary HF education series (eg., dieticians)
20. Inpatient consulting service
21. Inpatient patient education

repeat the information accurately, the information is rephrased. Then, the patient is asked to repeat the information again until the provider feels comfortable that the patient understood.

One method the MetroHealth System uses to foster self-care and adherence is a structured HF- specific education program. Three one-hour group sessions are taught by a nurse practitioner and dietician who utilize hands-on props, like food boxes. Patients who complete the program have a statistically significant gain in knowledge which translated into highly effective self-care behaviors. Eighty-four percent of patients did daily weight monitoring, 94 percent made efforts to eat a low sodium diet, and 91 percent rated themselves in being somewhat successful or very successful in following dietary guidelines.

Another strategy for fostering patient self-care and adherence is shared decision making. This is an ap-

proach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences. This extends beyond informed consent towards honoring informed patient preferences. Importantly, low health literacy will be a barrier to shared decision making. Shared decision making uses a three-step process of choice talk, option talk, and decision talk. Choice talk conveys that a choice exists, and it can be initiated by patient or provider. Option talk is informing the patient about the details about each treatment option. During decision talk, patients are supported to explore what matters most to them having become informed about the treatment options Decision support tools are used in option and decision talk.

Managed Care and HF

The management of HF is complex and fraught with barriers related to the advanced age and frequent comorbidities of many patients. Outcomes have been largely suboptimal to date, as hospitalization rates, morbidity, and mortality remain significant. From a plan perspective, collaborative care strategies, such as disease management and case management, in alignment with remote monitoring strategies and telemedicine, can help to improve the quality of care as well as associated outcomes in HF.

Close coordination with pharmacy management strategies can be used to ensure adherence by providers with prescribing GDMT and achieving target doses. Patient adherence monitoring programs can also be conducted in concert with pharmacy management.

Traditional agents for the treatment of HF, such as ACEIs, ARBs, and beta-blockers, are not typically managed aggressively because they are available generically and are relatively inexpensive even when branded. Conversely, newly available agents are being subjected to prior authorization (i.e., medical necessity) criteria by many plans based on drug indication and specific patient characteristics. In general, the criteria in place for ivabradine and sacubitril/valsartan are based on the FDA-labeled indications and the characteristics of patient populations enrolled in pivotal trials. Such criteria are in place to maximize the therapeutic potential of these agents and ensure that they are approved for patients who will have the greatest clinical benefit and lowest risk of adverse events.

Managed care plans can consider bundled payments when integrating pharmacy and medical services for HF. Bundled payment is a single payment to a provider for all services associated with a treatment or condition (for example, a HF hospitalization). The provider assumes risk; they can profit if cost of care is less than the bundled payment or lose. Bundled payments are often linked to meeting certain quality measures to ensure that delivery of high-quality care is maintained. The Bundled Payments for Care Improvement (BPCI) initiative from the Centers for Medicare and Medicaid is an example of one widespread model currently being evaluated in HF and other chronic conditions.

Overall, traditional models of medical and pharmacy management by clinicians and payers have not been very successful in improving outcomes and lowering costs. Managing HF will require innovative solutions and coordinated activity across the medical and pharmacy benefit.

Conclusion

HF is a complex and costly disease that is a challenge for payers to manage. Much of the cost of HF is due to in-patient hospitalization and subsequent readmissions (the revolving door). New treatments and updated guidelines-based care have the ability to improve outcomes, reduce hospitalizations and potentially improve cost. GDMT reduces the overall rates of mortality and sudden death related to HF. The guidelines must be systematically implemented and audited for compliance. ARNI should be considered in place of ACE/ARB in many patients with NYHA II-III HF. Heart rate is a therapeutic target, and ivabradine may augment the benefits of beta-blockers. Established therapies for HFrEF are under-utilized, particularly in advance of device implantation. More aggressive application of GDMT will continue to limit sudden death risk and reduce mortality in a cost-effective fashion. Traditional models of medical and pharmacy management by clinicians and payers have not been very successful in improving outcomes and lowering costs. Managing HF will require innovative solutions and coordinated managed care activity across the medical and pharmacy benefit.

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