Recent updates to guideline-directed medical therapy (GDMT) have the potential to help improve outcomes for patients with heart failure (HF). However, according to participants in an AJMC® Peer Exchange™, uptake of GDMT remains suboptimal because of high medication costs and concerns about the safety of starting or switching medications in patients hospitalized for HF. In a discussion moderated by Ryan Haumschild, PharmD, MS, MBA, director of pharmacy services at Emory Healthcare and Winship Cancer Institute in Atlanta, Georgia, the panelists described strategies to identify patients at risk for HF early in the disease process, improve uptake of GDMT in clinical practice, and optimize communication among members of a patient’s multidisciplinary team.

HF is caused by a structural or functional abnormality in ventricular filling or ejection of blood from the heart. Patients who have HF with reduced ejection fraction (HFrEF) have a substantially shorter lifespan compared with the age-matched general population, and hospitalization for HF is common and leads to poor outcomes. Therefore, early implementation of strategies to prevent HF progression, development of morbidities, and hospitalization are important to optimize outcomes.

The New York Heart Association (NYHA) classification is widely used by clinicians to assess symptoms and functional capacity for patients with symptomatic HF, and it is often used to identify patients who would be eligible for treatments. Clinicians typically classify patients at initial presentation and at follow-up intervals during treatment; although the classification is an independent predictor of mortality, it is subjective and has limited reproducibility and validity.

One shortcoming of the NYHA classification is that it does not evaluate the mechanism of HF or identify risk for HF in asymptomatic individuals. By contrast, the American College of Cardiology/American Heart Association (ACC/AHA) classification system focuses on categorizing patients based on the presence of symptoms, signs, and risk factors.
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on the development and progression of HF.\textsuperscript{1} Within the symptomatic stages, HF is also classified based on left ventricular ejection fraction (LVEF), because this measure influences prognosis and response to treatment and is used as a criterion for most clinical trials of HF.\textsuperscript{1} Although clinical trials vary in their cutoff values, the 2022 ACC/AHA guidelines use LVEFs of 40% or less, 41% to 49%, and at least 50% to correspond to HFrEF, HF with mildly reduced ejection fraction (HfmrEF), and HF with preserved ejection fraction (HFpEF), respectively.\textsuperscript{2}

The concept of the 4 pillars of HF therapy, initiated in parallel and very early in the course of HFpEF, was recently introduced as an optimal approach for treatment. The pillars are angiotensin receptor-neprilysin inhibitors (ARNIs), β-blockers (BBs), mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter 2 inhibitors (SGLT2is).\textsuperscript{3} A recent study that used overall trial–level estimates from randomized clinical studies of eplerenone (EMPHASIS-HF; NCT00232180), sacubitril-valsartan (PARADIGM-HF; NCT01035255), and dapagliflozin (DAPA-HF; NCT0306124) found that the HR for the improved treatment effect of quadruple pharmacologic therapy (ARNI, BB, MRA, and SGLT2i) on cardiovascular death or first HF hospitalization (ie, the primary end point) was 0.38 (95% CI, 0.30-0.47) compared with conventional therapy (an angiotensin-converting enzyme inhibitor [ACEi] or angiotensin receptor blocker [ARB] plus a BB).\textsuperscript{4} For a patient aged 55 years, the estimated event-free survival (based on the composite primary end point) was 14.7 years with quadruple therapy and 6.4 years with conventional therapy (difference, 8.3 years; 95% CI, 6.2-10.7 years), and the estimated overall residual survival was 17.7 years and 11.4 years with quadruple therapy and conventional therapy, respectively (difference, 6.3 years; 95% CI, 3.4-9.1 years).\textsuperscript{2}

The 2022 ACC/AHA guidelines were updated to define GDMT for HFrEF as including all 4 of these medication classes: ARNIs (or ACEi/ARBs if use of ARNIs is not feasible or is contraindicated), BBs, MRAs, and SGLT2is.\textsuperscript{5} In patients with HFrEF and NYHA class II or III symptoms, there is a class 1a recommendation for use of an ARNI and a class 1b recommendation to switch those on an ACEi or ARB to an ARNI. The guidelines include a value statement for this recommendation: “In patients with chronic symptomatic HFrEF, treatment with an ARNI instead of an ACEi provides high economic value.”\textsuperscript{6}

The recommendation for preferential use of an ARNI over an ACEi or ARB partially was based on findings from the PARADIGM-HF trial.\textsuperscript{7} Results demonstrated a lower rate of death from cardiovascular causes or hospitalization (primary end point) among patients with NYHA class II to IV HF who received sacubitril-valsartan compared with those using enalapril (HR, 0.80; 95% CI, 0.73-0.87; P < .001), suggesting that simultaneous inhibition of neprilysin and the angiotensin receptor yields better outcomes for patients with chronic HF than does inhibition of the renin-angiotensin system alone with an ACEi or ARB.\textsuperscript{8}

The recent inclusion of SGLT2is in GDMT for HFrEF was partially based on results from the EMPORER-Reduced trial (NCT03057977), which found a lower incidence of the primary composite outcome (death from cardiovascular causes or hospitalization for HF) with empagliflozin compared with placebo among patients with HF and an LVEF of 40% or less.\textsuperscript{9} The 2022 ACC/AHA guidelines also introduced value statements for recommendations evidenced by high-quality cost-effectiveness studies; ARNIs, BBs, and MRAs were noted to have high economic value for treatment of HFrEF, and SGLT2is were noted to have intermediate economic value for treatment of HFrEF.\textsuperscript{2}

The ACC/AHA guidelines also distinguished HfmrEF as a distinct clinical entity, with a class 2a recommendation for SGLT2is and class 2b recommendations for an ARNI (or ACEi/ARB), an MRA, or a BB. LVEF exists on a continuum in patients with HFmrEF; therefore, these individuals likely will benefit from GDMT.\textsuperscript{2} The guidelines also advise follow-up evaluation of GDMT in patients with HFmrEF to assess disease trends (ie, progression or improvement) and continuation of GDMT in patients who have improvement with treatment to prevent HF relapse and IV dysfunction (class 1b recommendation).\textsuperscript{7} For patients with HFpEF, the ACC/AHA guidelines state that SGLT2is may be beneficial (class 2a recommendation) and suggest that MRAs and ARNIs (or ARBs) be used in select patients, particularly those on the lower end of the LVEF spectrum (class 2b recommendation).\textsuperscript{2}
Consideration of an SGLT2i for HFmrEF and HFP EF was based on data from the EMPEROR-Preserved trial (NCT03057951), which found a lower incidence of a composite of cardiovascular death or hospitalization for HF with empagliflozin compared with placebo among patients with HF and an LVEF greater than 40% (HR, 0.79; 95% CI, 0.69-0.90; P < .001). Subgroup analyses showed that this outcome appeared to be particularly notable in patients with an LVEF of 41% to 49% (HR, 0.71; 95% CI, 0.57-0.88) and 50% to 59% (HR, 0.80; 95% CI, 0.64-0.99) and less so in those with an LVEF of 60% or greater (HR, 0.87; 95% CI, 0.69-1.10). Similarly, an exploratory analysis of data from the PARAGON-HF trial (NCT01920711) found a lower incidence of the primary outcome (composite of total hospitalizations for HF and death from cardiovascular causes) with sacubitril-valsartan compared with valsartan in patients with an LVEF of 45% to 57% (HR, 0.78; 95% CI, 0.64-0.95) and in women (HR, 0.73; 95% CI, 0.59-0.90), suggesting benefits of ARNi therapy in select patients with HFmrEF or HFP EF.

Stakeholder Insights

While the NYHA classification system is used to categorize HF, it focuses on symptomatic HF and does not address the disease mechanism or whether a patient is at risk for HF or has asymptomatic LV dysfunction, said Jim Januzzi, MD, a cardiologist at Massachusetts General Hospital and trustee at the American College of Cardiology, Boston, Massachusetts. By contrast, said Januzzi, the ACC/AHA staging criteria and guidelines emphasize the importance of identifying risk and treating asymptomatic HF in its early stages to prevent progression. He added that addressing the group of patients with HFmrEF, who were historically excluded from clinical trials, as a demographically and epidemiologically distinct population of patients with HF is a step forward in the ACC/AHA guidelines.

Although the 4 pillars of therapy for HF are largely the same across the spectrum of LVEF function, the benefits and strengths of recommendation vary, with recommendations strengthening at LVEFs of 40% or less, said Januzzi. According to Januzzi, the benefits observed with empagliflozin, even in patients with an LVEF greater than 50%, support treatment with an SGLT2i in those with HFP EF. The addition of MRAs (eg, spironolactone) and ARNIs (ie, sacubitril-valsartan) may also be beneficial in select patients with HFP EF or HFmrEF, notably women at the lower end of normal LVEF function, he said.

Inclusion of value statements in the 2022 ACC/AHA guidelines was an important step in recognizing the need to address the costs of medications with patients and payers, because patients may not be forthcoming about an inability to afford their medication, according to Jaime Murillo, MD, senior vice president and chief cardiometabolic health officer at UnitedHealth Group in Fort Lauderdale, Florida. Value statements in the guidelines also support the decision-making process for payers by providing data on the efficacy and safety of a medication in relation to its cost, said Murillo. Value statements are “incredibly important when those medications are put in the guidelines, because it gives the health plans the opportunity to say, ‘This is solid information [and] data, and we should make sure that patients have [access] to those medications,’” he said.

Although value-based care has always been at the forefront of his clinical practice as a hospitalist, Rohit Uppal, MD, MBA, SFHM, chief clinical officer at TeamHealth Hospitalist Services in Orlando, Florida, said that including value statements in the ACC/AHA guidelines increases transparency and supports clinicians in their value-based decision-making. “All of the goal-directed therapies that we target in our protocols are classified as high value,” he stated. “Our efforts really are focused on reaching higher levels of adherence to those evidence-based therapies.” Murillo added that HF tends to be chronic, often with multiple comorbidities and potential effects on quality of life. These factors, coupled with hospitalizations and readmissions, lead to high costs of HF-related and overall care. Therefore, he acknowledged that developing strategies to prevent HF is paramount.

“When we do our health economic outcomes analysis, we can separate the costs related to heart failure, [and] we can also look at the costs associated with that patient who [does not have heart failure alone], and you’ll be surprised at how high the burden is,” said Murillo. “People will be better served if we become experts on how to prevent heart failure.”

Uppal stated that the acute and postacute settings represent good opportunities to address costs and quality-of-life outcomes. At his institution, the specialties of emergency medicine, hospital medicine, postacute care, and virtual care are integrated, and leveraging these components is key to maximizing population health efforts for HF. Follow-up telemedicine visits from the emergency department are used to transition patients back home to help avoid unnecessary hospital admissions, and the hospital medicine team uses remote monitoring to assess patients. Some locations are also using the hospital-at-home model to potentially reduce costs and yield outcomes similar to those achieved by hospitalization. “When I think of our role as a hospital, I really emphasize the importance of a team-based approach,” said Uppal. “Managing congestive heart failure is just so complex and requires such a comprehensive approach. The key components are typically beyond the expertise of any single person on the team, [and it’s] certainly beyond the skills or knowledge of a hospitalist to meet [all] those needs. The ability to address all of the complex medical and social issues in this population is really the key.”

According to Uppal, team leaders and clinicians play an essential role in facilitating care coordination and patient education, addressing social determinants of health, and ensuring safe transitions of care between treatment settings. Januzzi added that the hospital is the most important setting to implement GDMT for patients with HF and that a team-based approach for follow-up that includes communication among hospitalists, primary care providers, and cardiologists is also important.

Uppal noted that a significant gap remains between GDMT and real-world clinical practice, but the 2022 ACC/AHA guidelines are likely to
encourage hospitalists to take proactive approaches to management, such as starting medication for hypertension in asymptomatic patients at risk for HF, switching to an ARNi in the hospital to treat active HF, and adding an SGLT2i for patients at high risk for readmission who are already on goal-directed therapy. Proactive identification of patients with stage A or B HF is also important in clinical practice, and treatment of risk factors such as hypertension, diabetes, and chronic kidney disease can help prevent development of symptomatic HF, said Januzzi.

### REAL-WORLD EVIDENCE AND TREATMENT PATTERNS IN HF

Although use of sacubitril-valsartan for select patients with HF is strongly supported by clinical trial data, the uptake of sacubitril-valsartan in real-world practice is modest, which may be due, in part, to concerns related to starting the drug in patients hospitalized for acute HF. However, results of the PIONEER-HF study (NCT02554890) indicate that starting sacubitril-valsartan in patients with HFpEF hospitalized for acute decompensated HF had similar safety and led to a significantly greater time-averaged reduction in N-terminal pro-B-type natriuretic peptide (NT-proBNP) level from baseline through weeks 4 and 8 compared with those who received enalapril (percent change, –46.7% vs –25.3%; ratio of change, 0.71; 95% CI, 0.63-0.81; P < .001). The greater reduction in NT-proBNP level with sacubitril-valsartan vs enalapril was observed as early as the first week of therapy (ratio of change, 0.76; 95% CI, 0.69-0.85). Similarly, results of the TRANSITION study (NCT02661217) showed that the target dose of sacubitril-valsartan was achieved by a similar proportion of patients hospitalized for acute decompensated HF who were started on the drug before discharge and those who received the drug 1 to 14 days after discharge (45.4% vs 50.7%; relative risk ratio, 0.90; 95% CI, 0.79-1.02). The rates of adverse events (AEs), serious AEs, and temporary and permanent treatment discontinuations over 10 weeks were similar between groups. The authors of the study noted that the ability to initiate, increase, and maintain the sacubitril-valsartan dose was similar between patients who were naïve to ACEi or ARB therapy and those who were taking ACEis/ARBs at the time of hospital admission; further, the tolerability for sacubitril-valsartan appeared to be similar to that of BBs and ACEis or ARBs reported in the real-world setting. They concluded that results from the TRANSITION study support those from PIONEER-HF, suggesting that initiation of sacubitril-valsartan is feasible prior to or soon after hospital discharge in patients hospitalized for acute decompensated HF.

The reduction in NT-proBNP level observed with sacubitril-valsartan may have long-term clinical implications for cardiac structure and function, according to findings from the PROVE-HF trial (NCT02887183). Significant correlations were noted between the change in log NT-proBNP concentration and markers of cardiac remodeling (LVEF [r = –0.381; IQR, –0.448 to –0.310; P < .001], LV end-diastolic volume index [r = 0.320; IQR, 0.246-0.391; P < .001], LV end-systolic volume index [r = 0.405; IQR, 0.335-0.470; P < .001], left atrial volume index [r = 0.263; IQR, 0.186-0.338; P < .001], and ratio between early transmitial Doppler velocity and early diastolic annular velocity [r = 0.269; IQR, 0.182-0.353; P < .001]) in patients with HFpEF. The study authors acknowledged that the reverse cardiac remodeling observed in the trial may explain the mechanism of action for sacubitril-valsartan in patients with HFpEF and that the markers of reverse cardiac remodeling may identify patients with improved prognosis on ARNi therapy.

Improving LVEF and reversing cardiac remodeling through ARNIs and other GDMT that reduce HF hospitalizations may have implications on the costs of care. In a systematic review, HF-specific hospitalizations were found to be a major driver of the total cost of care. The analyses estimated that the median annual cost of HF-specific hospitalizations per patient was $13,418 (2019 US$) (interquartile limits [IQL], $11,125-$15,667), and the median total annual medical cost was $24,383 per patient (IQL, $20,713-$40,619). The median HF-specific hospitalization cost per patient was also higher among patients with comorbidities ($14,015; IQL, $11,769-$20,373), and the cost per hospitalization episode was up to 100% higher in patients with HFpEF compared with those with HFpEF. Although the authors of the study noted that there is substantial heterogeneity in HF-related costs (partially due to the diverse range of medical concerns among subgroups of patients and partially due to discrepancies in study design and reporting), HF hospitalization costs are a predominant source of costs and a common driver in cost-effectiveness models for HF.

### Stakeholder Insights

Patients who have been hospitalized for HF often have multiple comorbidities, and clear communication among the hospitalist, cardiologist, and primary care provider is essential for adequate care and initiation of GDMT, said John E. Anderson, MD, physician of internal medicine and diabetes at TriStar Centennial Medical Center, in Nashville, Tennessee. "It’s no longer good enough to just send a message through an electronic medical record," he said. "It is incumbent upon us to pick up the phone and talk to each other when we have those transitions and to work actively with cardiologists and hospitals." Januzzi acknowledged that starting all 4 drug classes simultaneously is usually not feasible, because identification of a medication associated with a particular AE may be difficult. However, the medications can be introduced in rapid succession to get a patient on all 4 classes within a couple of weeks, he said. Januzzi generally initiates sacubitril-valsartan with a BB and avoids starting it with an MRA or SGLT2i, because these latter 2 and sacubitril-valsartan can have renal AEs. "The key is to not so much get 1 drug up to whopping doses before we get another 1 started," he stated. "A little bit of everything is far more important than a whole lot of 1 drug, and then you can focus on titration once you’ve initiated [therapy]."

Uppal said that the treatment goals for HFpEF and HFpEF are similar and focus on reducing symptoms, improving quality of life, and reducing costs are a predominant source of costs and a common driver in cost-effectiveness models for HF.

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**People will be better served if we become experts on how to prevent heart failure.**

Jaime Murillo, MD
UnitedHealth Group
Fort Lauderdale, FL
risk for hospital readmission, but the evidence is less clear on whether interventions reduce mortality in patients with HFpEF. However, he indicated that many patients with HFpEF also have comorbidities (eg, atrial fibrillation, coronary artery disease, and diabetes), and they can be managed with a drug that is also indicated for HF (eg, an SGLT2i for diabetes or an MRA for hypertension).

The effect of early initiation of GDMT on total cost of care and patient outcomes is complex, but the lower likelihood of hospitalization is likely to reduce the cost of care, said Murillo. Many opportunities remain to personalize the treatment approach, and Murillo emphasized the importance of figuring out how to use factors such as social determinants of health, socioeconomic status, and patients’ understanding of their disease to identify those who would benefit from early initiation of medications to prevent HF admissions. He also indicated that it is critical to use real-world evidence to assess utilization and effectiveness of interventions (eg, using SGLT2is and ARNis in different patient populations in a relatively short timeframe) rather than waiting several years for data from randomized controlled trials.

Although Januzzi has observed a shift toward using sacubitril-valsartan and noted the superior outcomes compared with ARB or ACEi therapy, uptake in clinical practice has been relatively modest, in part because of the higher cost of sacubitril-valsartan. The ACC/AHA guidelines state that an ACEi or ARB can be used in place of an ARNi for renin-angiotensin system inhibition.1 However, Januzzi generally starts patients on sacubitril-valsartan unless there is a specific reason to avoid it. Anderson added that switching to an ARNi from an ACEi or ARB is appropriate and feasible in most patients with HFpEF, and increased awareness among primary care providers is likely to further improve uptake, although he has observed a significant increase in uptake at hospital discharge and among cardiologists. “At our institution, the hospitals and the cardiologists work in tandem [and] have great communication,” said Anderson. “Even at week 1, you see NT-proBNP levels improving.”

Uppal added that although the transition to an ARNi has not been as robust as he would have hoped, the data from the TRANSITION trial—showing the safety of starting ARNis once patients have stabilized in the hospital—are likely to give hospitalists the confidence to make the switch from an ACEi or ARB to an ARNi in the hospital. Januzzi added that the improvements continue for several months after the initiation of sacubitril-valsartan, and this is also observed with other medications. “You can tell your patients that [they] can continue to expect ongoing improvement, and this is not just with drugs like sacubitril-valsartan,” he said. “With [a] well-dosed β-blocker, you see very similar benefits. With SGLT2is, we recently showed that the NT-proBNP reductions continue out to a year after [starting a patient] on empagliflozin, and improvements in health status extend out well beyond that period of time.”

Januzzi added that although the PARAGON-HF trial results did not show significant improvements in the number of HF hospitalizations and cardiovascular deaths in the whole population, the improvements observed in certain subgroups of patients (notably women and patients with an LVEF of 55% or lower) suggest that an individualized approach is best to assess whether a patient with HFpEF or HFmrEF would benefit from sacubitril-valsartan. For example, Januzzi said he would be more likely to consider using sacubitril-valsartan in women with a LVEF of 55% or greater than in men with a similar LVEF, and he “definitely” considers it for patients who have been hospitalized.

Although empagliflozin has shown clinical benefits in HFrEF and HFpEF, Anderson said that early initiation may not be advisable in certain patients, such as those who are hospitalized with euglycemic diabetic ketoacidosis or who have recurrent genital mycotic infections. However, he noted that genital mycotic infections did not recur in the majority of patients in SGLT2i clinical trials who experienced this AE. Anderson added that uptake of SGLT2is may be suboptimal, because some physicians are concerned about needing to adjust a patient’s other glucose-lowering drugs; however, he noted that adding an SGLT2i often does not require such adjustment, because the reductions in hemoglobin A1c levels with SGLT2is are modest.

Murillo acknowledged that efforts have been made by accountable care organizations to identify patients at risk and to ensure that transitions from hospitalization to specialist care are quicker and that patients receive GDMT. He added that aiming for value-based care, rather than starting with the lowest-cost medication, would be ideal for managing patients with HF. “If you’re in an environment where there is a more of a team approach, it’s not about how much you’re able to bill for a visit, or for a procedure, but, rather, ‘Will this person in front of me be healthier within 6 to 12 months?’” he said. “The patient gets better, but, also, the total cost of care will be lower.”

**ACCESS AND AFFORDABILITY IN HF: STAKEHOLDER INSIGHTS**

Hospitalists can take into consideration numerous variables—including NT-proBNP level, estimated glomerular filtration rate, cardiac telemetry data, LVEF, the need for inotropes, NYHA classification, and prior patient response to medical therapy—that, along with social determinants of health, can help identify those with HF who are at high risk for poor outcomes, said Uppal. Other metrics that he monitors include inpatient length of stay; rates of hospital readmission, mortality, and referral to cardiologist or hospice and palliative care; and patient experience scores, which are a strong driver of patient adherence after hospital discharge. Because it is challenging for a hospitalist to address all of the medical and social issues of patients with HF, Uppal emphasized the importance of including advanced care planning to improve quality of life and management of care costs and to have a multidisciplinary management team that includes nurses, case managers, pharmacists, social workers, nutritionists, and palliative care doctors in addition
to hospitalists and cardiologists. Murillo added that payers also make important contributions to the care team for patients with HF. They have initiated pilot projects for remote patient monitoring and for working with accountable care organizations, health systems, and employers to improve patient care and reduce complications. “It’s not just about negotiating a contract. It really is, ‘What can we do together to make our patients better?’” said Murillo.

Anderson said that his institution generally does a good job at implementing GDMT for hospitalized patients with HF, but improvement is needed to generate a systematic approach, particularly in the outpatient setting. Regarding possible ways to increase the uptake of GDMT, Januzzi suggested electronic health record prompts or a smartphone application that recommends medications, but he stressed that educating clinicians is ultimately most important. “You can prompt all day, but if they don’t make the changes, it won’t necessarily improve care,” he said.

Patients with HF tend to have multiple comorbidities, and effective treatments are often underutilized out of concerns for safety and patient adherence, said Uppal. Therefore, care managers, pharmacists, and home visits to promote adherence, along with effective communication between clinicians during transitions of care and effective management of comorbidities, are important to reduce the risk for hospital readmission.

The high cost of ARNi and SGLT2i drugs can also present a barrier for some patients, said Anderson. Although these drugs are generally covered by Medicare and commercial insurance, patients on Medicare who have reached the coverage gap may have difficulty paying for their HF medications, because they may be responsible for up to 25% of the cost of brand-name drugs. (The coverage gap is a temporary limit on what the plan covers for medications after the patient and the plan spend a certain amount on covered drugs and before reaching the catastrophic coverage period; the amount for 2022 is $4430.12.) “This is probably 1 of the most heartbreaking struggles that I deal with at work every single day, when I have patients telling me that they have to make choices [as far as] which medications they’re going to take,” said Januzzi. “It’s imperative that we not only recognize that there’s a social commitment to our patients that we should be making, but, in a larger sense, [that] the health care system can only benefit from our patients receiving these medications, because it reduces the huge costs and care related to heart failure hospitalization and all the morbidity that accompanies that.” Strategies that Januzzi uses to minimize patient cost burden include consulting with a pharmacist, social worker, or patient navigator to identify patient assistance programs; obtaining a higher dose and pill splitting (if feasible); and identifying areas in which care can be streamlined (eg, using an SGLT2i instead of a dipeptidyl peptidase-4 inhibitor for patients with comorbid diabetes).

### CLOSING REMARKS

A proactive approach to identifying patients at risk for HF, educating providers involved in caring for patients with HF on the optimal GDMT, and implementing team-based management that involves effective communication across multiple specialties is essential in moving forward. Additionally, more research is needed in populations traditionally underrepresented in clinical trials—particularly hospitalized patients with multiple comorbidities, older patients, Black patients, and women. In addition, strategies to improve adherence and empower patients in the real world (particularly in those with complex medication regimens) are important. “With the growing tide of HF in the current health care system, it’s all hands on deck,” said Januzzi. “Everyone needs to know how to use these therapies and apply them effectively to reduce the risk for our patients.”

### REFERENCES
