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# Innovation in Ambulatory Care of Heart Failure in the Era of Coronavirus Disease 2019



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## KEYWORDS

• Ambulatory • Care optimization • COVID-19 • Guideline-directed medical therapy • Heart failure

## KEY POINTS

- Major gaps exist in the implementation of guideline-directed medical therapy for heart failure (HF). Ambulatory care optimization should focus on rapid and successful implementation of effective therapies.
- HF is associated with high comorbid disease burden. Ambulatory management of comorbidities should be incorporated into HF disease management programs.
- Optimizing ambulatory HF care will require a multidisciplinary team to address therapeutic optimization, active comorbid disease management, and nutrition and structured exercise-based interventions.

## INTRODUCTION

Heart failure (HF) is a chronic disease state that affects up to 6 million Americans; the prevalence is poised to rise in upcoming years given population aging and adverse trends in cardiometabolic comorbidities.<sup>1</sup> HF is a major contributor of morbidity and mortality in the United States, with 1 in 9 death certificates mentioning HF and more than 58,000 deaths attributed to HF annually.<sup>1</sup> The natural history of HF with reduced ejection fraction (HFrEF) has been significantly disrupted with the sequential development and demonstration of benefit of 6 distinct classes of disease-modifying therapies: angiotensin-converting enzyme inhibitors (ACEi), angiotensin II receptor blockers (ARB), angiotensin receptor-neprilysin inhibitors (ARNI),  $\beta$ -blockers, mineralocorticoid receptor antagonists (MRA), and most recently, the

sodium glucose cotransporter-2 inhibitors (SGLT2i). However, despite these recent advances, fewer than 1% of patients with HF are simultaneously treated with target doses of multiple evidence-based classes (ACEi/ARB/ARNI,  $\beta$ -blockers, and MRA).<sup>2–4</sup> In addition, as there are currently no approved therapies for patients with HF with preserved ejection fraction, its management has relied on the rigorous targeting of key comorbidities and effective hemodynamic and volume-control strategies.

Although focus on optimization around the time of hospitalization represents an important target of care efforts, a large segment of the HF population lives in community settings, at times with limited care access. Most patient-physician interactions occur in ambulatory clinics, including those that span primary care, cardiology, and advanced HF. As such, optimizing care pathways in the

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ambulatory setting is a particularly promising area of care innovation. In addition, the emergence of the Coronavirus Disease 2019 (COVID-19) pandemic has threatened traditional care approaches, limiting health care access and interactions. The introduction of new technologies and expansion in insurance coverage of telehealth options, combined with team-based multidisciplinary efforts, have the potential to provide a lasting impact on care delivery in ambulatory practice.

### GAPS IN PROVISION OF EVIDENCE-BASED THERAPIES

Data from the Changing the Management of Patients with Heart Failure (CHAMP-HF), Contemporary Drug Treatment of Chronic HF (CHECK-HF), and Quality of Adherence to guideline recommendations for life-saving treatment in HF survey (QUALIFY) registries suggest there are important gaps in the use and dosing of key elements of guideline-directed medical therapy (GDMT) in clinical practice.<sup>5–9</sup> Despite a robust evidence base and guideline documents supporting full implementation of GDMT at target doses, the administration and uptitration of these therapies in patients with HFrEF are suboptimal<sup>10</sup> (Table 1).

### IMPLEMENTING GUIDELINE-DIRECTED MEDICAL THERAPY

Given the multifaceted interactions between patients with HF and the health care system, team-based care approaches to GDMT optimization may be particularly valuable.<sup>11</sup> One strategy to improve delivery of GDMT is using non-physician medical staff under the guidance of HF specialists to engage in more active and frequent therapeutic changes. For instance, clinical pharmacists are experienced members of inpatient and outpatient interdisciplinary care teams and may serve as an

important resource to aid in earlier initiation and uptitration. A model of pharmacist involvement in HF consult services in the inpatient setting has led to increased use of GDMT.<sup>12</sup> In the outpatient setting, one small pilot study used pharmacists to help manage dose titrations of GDMT. Despite small sample size, this intervention led to target dose  $\beta$ -blocker titration in 78% of patients and a significant reduction in all-cause hospital admissions.<sup>13</sup> Other studies have also shown reduction in hospital readmissions for HF when pharmacists are used to assist GDMT implementation in the outpatient setting.<sup>14</sup> Similarly, nursing-directed clinics have also been shown to increase adherence and optimize titration of GDMT.<sup>15,16</sup> Organizing these non-physician providers in GDMT-specific clinics (Fig. 1) represents a strategy to de-link usual care (which may focus on acute care needs and decongestion) and therapeutic optimization.<sup>17,18</sup> Randomized clinical trials examining an early intensive GDMT uptitration strategy as compared with usual care are under way (NCT03412201).

### High-Quality Transitions in Care

Quality improvement programs have been previously implemented to attempt to improve GDMT uptake in patients admitted with HF. The American Heart Association's Get with the Guidelines Heart Failure (GWTG-HF) program is one such example.<sup>19</sup> Hospitals participating in the GWTG-HF program had higher use of GDMT (notably ACEi) and slightly improved readmission rates.<sup>20,21</sup> The GWTG-HF program expands on the progress of preceding initiatives including the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) program, which focused on implementing high-quality care at hospital discharge.<sup>22</sup> Process improvement initiatives embedded within

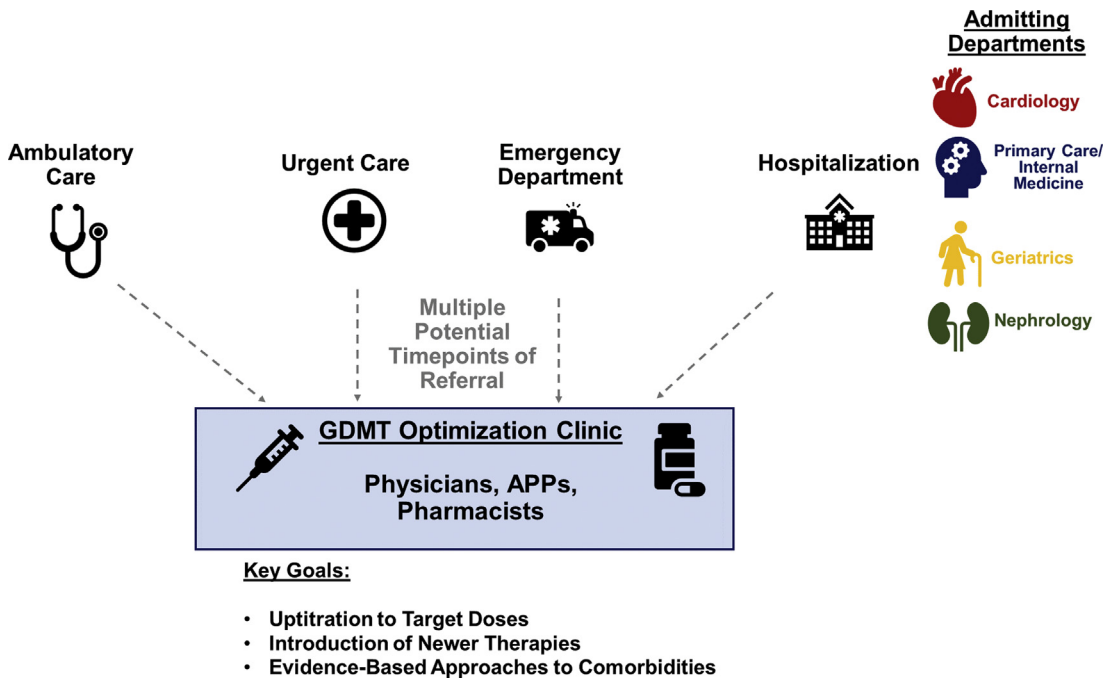
Table 1

Incomplete use and target dose achievement of guideline-directed medical therapy for heart failure with reduced ejection fraction in usual care settings globally

Registry	On/Adherent to Therapy, %			$\geq 50\%$ Target Dose, <sup>a</sup> %			$\geq 100\%$ Target Dose, <sup>a</sup> %		
	ACEi/ARB/ARNI	Beta Blocker	MRA	ACEi/ARB/ARNI	Beta Blocker	MRA	ACEi/ARB/ARNI	Beta Blocker	MRA
CHAMP-HF	73.4	67	33.4	83.1	72.5	98.2	16.8	27.5	76.6
CHECK-HF	84	86	56	76	55	97.9	43.6	18.9	52
QUALIFY	62	79	86	74	60	76	22.7	14.8	70.8

**Abbreviations:** ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CHAMP-HF, changing the management of patients with heart failure; CHECK-HF, Contemporary Drug Treatment of Chronic HF; MRA, mineralocorticoid receptor antagonist; QUALIFY, quality of adherence to guideline recommendations for life-saving treatment in HF survey.

<sup>a</sup> Percentages reported as a proportion of patients on therapy.



**Fig. 1.** Innovative care delivery pathway to optimize GDMT in HF. APP, advanced practice provider. (From Myhre PL, Januzzi JL Jr, Butler J, et al. De novo heart failure: where the journey begins. *Eur J Heart Fail* 2019, 21(10):1245–7; with permission.)

OPTIMIZE-HF were shown to be associated with reduced HF and cardiovascular readmission rates.<sup>23</sup> In parallel with these “real-world” clinical programs, traditional randomized trials have demonstrated that in-hospital initiation of evidence-based therapies is not only safe, but may lead to improved postdischarge use and therapeutic persistence.<sup>24–26</sup> However, patient-centered transitional care alone, such as evaluated in the Patient-Centered Care Transitions in HF (PACT-HF) service model, has not been associated with improved postdischarge outcomes.<sup>27</sup> In the PACT-HF trial the intervention group incorporated a hospital nurse navigator to facilitate a needs-based assessment and intervention reflecting self-reported quality of life, education, patient-centered discharge summary, multidisciplinary referrals, and family physician follow-up at the time of discharge. These findings highlight the importance of linked programs specifically designed to improve GDMT uptake during HF hospitalization, which seamlessly continue acceleration of therapy in the post-hospitalization period.

**Telemedicine and Remote Health Management**

Telemedicine represents an emerging strategy for optimizing GDMT and HF care at a more rapid pace, especially for patients who live in rural

settings or those with limited access or high barriers to traditional clinical visits. These approaches may be particularly relevant in an era of COVID-19 and associated need for social distancing, further limiting contact with traditional ambulatory clinic settings. Indeed, the Centers for Medicare and Medicaid Services has expanded coverage to Medicare telehealth services in March 2020 in response to the escalating COVID-19 pandemic.

Although the results have been mixed in other clinical settings, studies suggest that telemedicine may facilitate improved patient interaction that may in turn promote GDMT initiation and uptitration at a scale difficult to obtain with traditional in-person visits.<sup>28–30</sup> A meta-analysis of 8323 patients across 25 randomized controlled trials suggested a reduction in all-cause mortality with telemonitoring (monitoring blood pressure, weight, electrocardiographic strips) compared with usual care among patients with HF.<sup>31</sup> In the Telemedical Interventional Management in Heart Failure II (TIM-HF2) trial conducted in Germany, patients with HF were randomized to telemonitoring strategy or usual care.<sup>29</sup> The telemonitoring group was given an electrocardiogram device, blood pressure measuring device, electronic scale, oximeter, and a mobile phone to communicate remotely with the clinic. The telemedical data were transmitted daily and the patient was managed according to a set algorithm. Telemonitoring reduced

cardiovascular mortality and hospitalization for HF after 12 months of follow-up.<sup>29</sup> Given improvement in technology and continuous assessment, using wearable technology offers a new and convenient method for managing HF in the outpatient setting and particularly alerting providers when hemodynamics may allow for more aggressive GDMT. For example, one study provided participants a smartphone and a smartwatch along with an application that tracked participant activity data and required them to input daily self-measured blood pressure and body weight. Although this study was limited in size, a significant increase in quality of life and performance status was reported.<sup>32</sup> In patients with advanced HF, monitoring of pulmonary artery (PA) and intracardiac pressures via implantable devices has already been shown to reduce HF hospitalizations.<sup>33,34</sup> For example, the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) trial showed improved clinical outcomes with longitudinal assessment and access to real-time PA pressure measurements that may be due to improved GDMT in the monitored group.<sup>33</sup> Given interconnectivity and telecommunication advances in the modern era, telemedicine is poised to become increasingly important in the management of chronic diseases such as HF. For example, the upcoming HF Study to Evaluate Vital Signs and Overcome Low Use of GDMT by Remote Monitoring (HF-eVOLUTION) trial will be evaluating the effectiveness of vital signs monitoring via wrist watch on GDMT use and may shed light on this novel strategy (NCT04292275). Similar telehealth solutions should be developed and empirically evaluated to determine if implementation may help improve GDMT use.

## COMORBIDITY MANAGEMENT IN HEART FAILURE

Patients with HF often have comorbid noncardiac conditions that contribute to morbidity, mortality, and impaired health-related quality of life. In one study, more than 80% of patients with HF had at least 1 noncardiovascular comorbid condition and 25% had more than 3.<sup>35</sup> Patients with HF and comorbid conditions have worse outcomes, including increased mortality and HF admissions.<sup>35</sup> Chronic obstructive lung disease (COPD) and anemia have independently been associated with increased HF admissions and poorer outcomes.<sup>36</sup> Patients with comorbid conditions also had more severe HF symptoms, including fatigue, dyspnea, pain, and anxiety, which may collectively contribute to worse quality of life.<sup>37</sup> Therefore,

comprehensive ambulatory management of patients with HF should include active surveillance and management of comorbid conditions. In addition, added comorbidity burden increased polypharmacy and may adversely affect adherence. Evaluation and early treatment or prevention of comorbid conditions are crucial to prevent potential exacerbation of HF and provide comprehensive cardiopulmonary and systemic care.

The most commonly identified comorbidities in patients with HF are diabetes mellitus, COPD, chronic kidney disease, and anemia.<sup>35,37–39</sup> In patients with diabetes mellitus (both with and without HF), new therapeutic options have emerged, including SGLT2i. SGLT2i has been found to decrease HF events in patients with type 2 diabetes mellitus.<sup>40–44</sup> The landmark Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction (DAPA-HF) trial additionally demonstrated that dapagliflozin may be helpful in the treatment of patients with established HFrEF.<sup>45</sup> Cardiologists will need to take a more active role in prescribing these therapies, which have traditionally been considered only for their glucose-lowering potential. COPD is comorbid with HF and has been associated with increased mortality and hospitalization.<sup>46,47</sup> In the context of multiple intersecting comorbidities, programs designed to aid patients in medication adherence (and avoidance of potentially harmful or unnecessary therapies) will become increasingly important, particularly as medication burden increases.<sup>48</sup>

Last, depression is an often-overlooked comorbidity in patients with HF. Depression is comorbid in approximately 22% of patients with HF and has been associated with poor health-related quality of life and is an independent risk factor for subsequent cardiovascular events.<sup>49,50</sup> Importantly, depression may adversely impact therapeutic and lifestyle adherence.<sup>51</sup> Therefore, early screening and mental health support may be an additional avenue to improve adherence in patients with HF with concomitant depression.

## VACCINATION

Vaccination is an important part of global prevention, even more so in patients with chronic diseases such as HF. In particular, vaccination against pulmonary pathogens (influenza and pneumococcus) in HF has some promise in improving outcomes, although no large clinical trials have been reported yet.<sup>52</sup> There are many plausible mechanisms by which influenza infection may promote worsening HF, including proinflammatory acceleration of atherogenesis in addition to direct myocardial depressant effects of inflammatory cytokines.

Routine early influenza vaccination has been shown to be effective in patients with atherosclerotic vascular disease and recent acute coronary syndrome.<sup>53</sup> In addition, recent data suggest that early, well-matched consistent influenza vaccination in patients with HF may improve clinical outcomes and reduce rehospitalization rates.<sup>54</sup> Data from a large randomized clinical trial also showed an association between influenza vaccination and improved cardiovascular events.<sup>55</sup> Despite this, usual care evidence suggests major gaps in influenza vaccination rates in the United States, with increasing refusal rates.<sup>56</sup> In addition, centers performing well with respect to influenza vaccination in patients with HF also performed well with respect to other HF quality measures, suggesting that particular centers may have integrated structured approaches to influenza vaccination administration into traditional HF disease management programs. Despite common sense indication for influenza vaccination and clear biological plausibility for benefit in patients with established cardiopulmonary disease, a focal anti-vaccination contingent and strong personal feelings and fears with regard to influenza vaccination may, in part, explain disappointing vaccination rates among patients with cardiovascular disease. New implementation avenues, particular those that may involve direct, patient-facing behavioral economic nudges, are needed to better understand barriers for nonvaccination and strategies for improvement. These learnings from vaccination efforts for seasonal influenza may be effectively translated to overcome upcoming challenges in disseminating effective vaccines against COVID-19 (once developed and available).

## LIFESTYLE INTERVENTIONS IN AMBULATORY PRACTICE

As with many chronic cardiometabolic diseases, lifestyle modification is critical as a central tenet of disease management. HF is no exception, and thus lifestyle modification interventions should be part of every outpatient HF program and clinic. Structured exercise programs are one such intervention that has been proposed in HF, particularly given the overlap among HF, metabolic syndrome, and obesity, all of which are potentially mitigated by exercise and accelerated basal metabolic rates.<sup>57</sup> The Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) trial investigated the health effects of an exercise training program in patients with HFrEF.<sup>58</sup> This trial showed that an exercise training program in patients with HF is safe and may have modest reductions in all-cause and cardiovascular mortality and hospitalization.<sup>58</sup> Patients in the exercise

group also had improved 6-minute walk distance and cardiopulmonary exercise duration. Furthermore, this improvement in 6-minute walk distance and cardiopulmonary exercise duration was similar across baseline physical activity levels.<sup>59</sup> One small study showed that a multidisciplinary clinic with cardiac rehabilitation, dietitians, psychologists, and nurse educators reduced HF hospitalization.<sup>60</sup> In addition to exercise, diet is important for HF and health overall.<sup>61</sup> HF is a catabolic state and malnutrition and cachexia are poor prognostic factors in HF.<sup>62</sup> One small upcoming study will investigate the role of diet optimization via nutrition education on nutritional and quality-of-life outcomes in patients with HF (NCT03845309), although larger trials are needed to investigate disruptive nutritional programs that may benefit patients with HF.

## SUMMARY

Advancement in therapeutic options in recent decades have afforded us several avenues and tools for care optimization, including pharmacologic therapies, novel technology-based monitoring, and nonpharmacological interventions, such as vaccination, nutrition, and structured exercise-based approaches. Delivering high-quality HF care in a fragmented health system is increasingly challenging and likely ineffective; integrated ambulatory clinics designed around multidisciplinary teams including physicians, advanced practice providers, clinical pharmacists, nurses, nutritionists, exercise physiologists, and social workers, among others, are needed to provide care that is effective and optimal. These approaches, coupled with telehealth solutions, may minimize multiple health care interactions and travel for patients at risk for COVID-19. Furthermore, greater study is needed with regard to how these teams may effectively partner and engage patients to be champions of their own health, empowering them to seek new interventions, technologies, and lifestyle changes. Overall, the ambulatory setting (extending well beyond the walls of a single clinic) offers a comprehensive environment for care optimization. Ambulatory innovations in HF care must focus not only on disease-modifying interventions, but also on comprehensive HF and comorbid care designed to relieve symptoms, improve functional status, and optimize nutrition and weight management.

## DISCLOSURE

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