

**PACE**

Pharmaceutical Assistance  
Contract for the Elderly



Balanced information for better care

# Heart failure

## Improving outcomes in primary care



# Heart failure prevalence is increasing, but there are opportunities to improve outcomes

Heart failure hospitalizations have been decreasing because of both more effective care and changes in reimbursement.<sup>1,2</sup> But despite recent improvements, heart failure remains a leading cause of hospitalization.

Evidence-based management is guided by the ejection fraction.

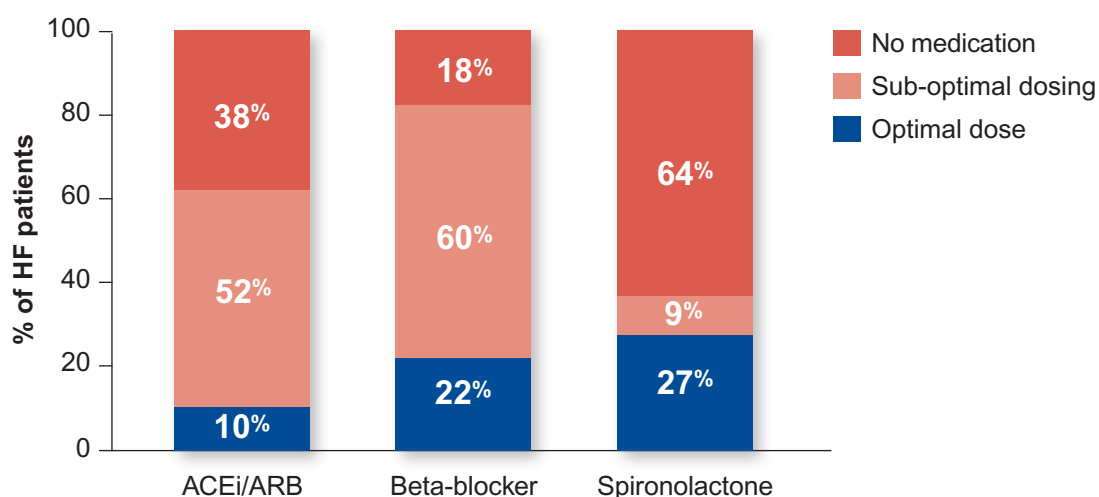
**TABLE 1.** Classification of heart failure based on patient's EF<sup>3,4</sup>

Heart failure with <b>reduced</b> ejection fraction (HFrEF)	≤ 40% EF	<b>systolic HF</b>
Heart failure with <b>preserved</b> ejection fraction (HFpEF)	≥ 50% EF	<b>diastolic HF</b>

Patients with **mid-range** EF (i.e., 41-49%) should be treated like patients with reduced EF. In patients whose EF improves on treatment, continue medications based on the initial EF.

Medication use can be substantially improved in most patients with HFrEF.

**FIGURE 1.** Most patients with reduced EF are not on optimal doses of the evidence-based treatments for heart failure within one year after diagnosis.<sup>5</sup>



Life-saving therapies are under-utilized in typical U.S. practice. Prescribing two or three HF medications reduced the likelihood of death a year after a heart failure hospitalization by 44% and 54%, respectively, compared to the risk of death in patients not taking these drugs.<sup>6</sup>



# Base management on clinical stage

**FIGURE 2.** Identifying the stage of heart failure should guide management.<sup>3,4</sup>

	STAGE	DESCRIPTION	GOAL
Prevention	<b>STAGE A</b>	<b>At risk for developing HF</b>	Prevent HF by treating risk factors, such as hypertension and diabetes.
	<b>STAGE B</b>	<b>Asymptomatic with structural heart disease*</b>	Treat with beta blockers and ACE inhibitors or ARBs <sup>†</sup> to prevent progression to symptomatic HF.
Heart failure	<b>STAGE C</b>	<b>Symptomatic prior or current symptoms of HF</b>	Use evidence-based treatments to reduce symptoms and improve outcomes.
	<b>STAGE D</b>	<b>Refractory or advanced HF</b>	Refer to specialists for advanced therapies when indicated and discuss goal-directed care with patients.

Source: American College of Cardiology Foundation and American Heart Association

\* **Structural heart disease:** left ventricular (LV) hypertrophy, LV dysfunction, prior myocardial infarction, or valvular disease

<sup>†</sup> **ACE:** Angiotensin-converting enzyme; **ARB:** Angiotensin receptor blocker

# Prevent progression to heart failure

## STAGE A

At risk for heart failure

**Treating risk factors can reduce the likelihood of developing heart failure.**

- **Predisposing conditions:** coronary heart disease, hypertension, diabetes, chronic kidney disease, obesity, obstructive sleep apnea
- **Behaviors:** smoking, lack of physical activity, alcohol consumption, diet with excessive calories and/or salt, non-adherence to medications

## STAGE B

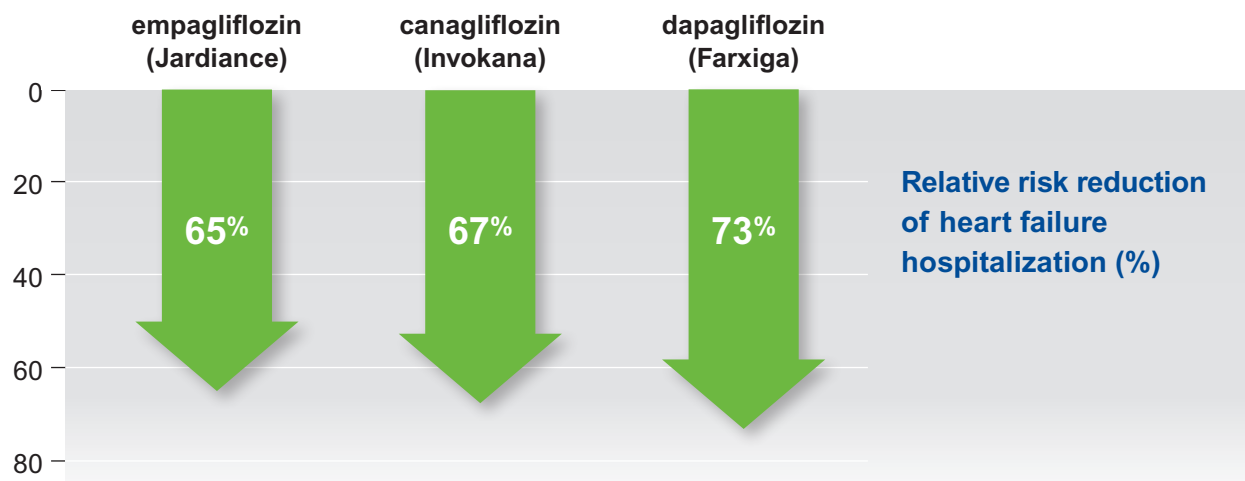
Asymptomatic patients with structural heart disease or with reduced EF

**Medication and other interventions can slow progression to symptomatic disease.**

- In patients with reduced EF, prescribe an ARB or ACE inhibitor and a beta-blocker.
- Optimize medical management for secondary prevention in patients post-myocardial infarction (e.g., statin, antiplatelet therapy, beta blocker, ACE inhibitor/ARB).
- Identify structural heart disease, such as significant mitral regurgitation, and refer to a specialist to address it when indicated.

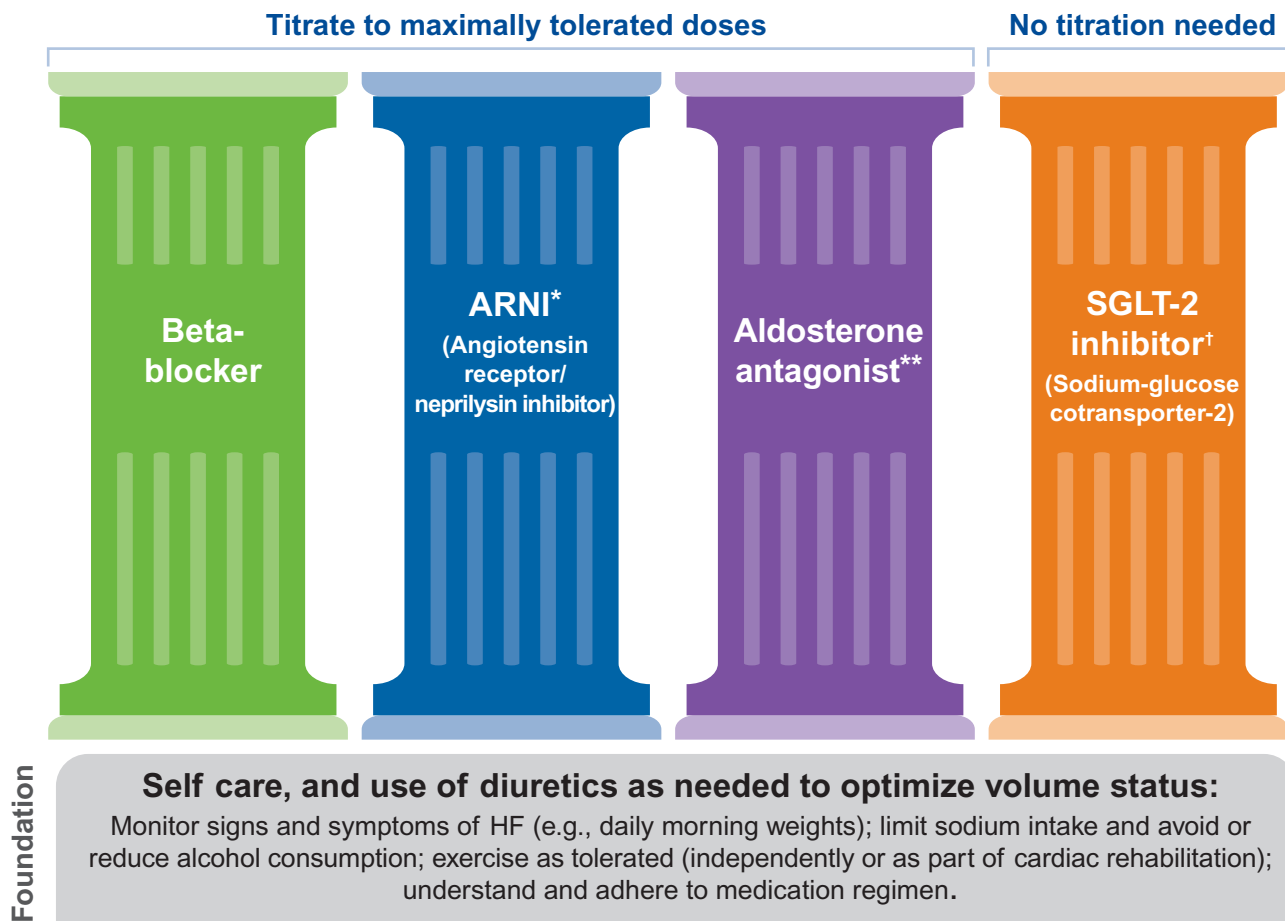
**In patients with diabetes, prescribe an SGLT-2 inhibitor if cardiovascular disease or other important risk factors are present.**

**FIGURE 3.** Sodium-glucose cotransporter-2 (SGLT-2) inhibitors prevent heart failure hospitalization in patients with diabetes.<sup>7-9</sup>



# Pharmacotherapy of patients with HFrEF

**FIGURE 4.** The pillars of drug therapy for patients with reduced ejection fraction<sup>10</sup>



\*Can use ACE inhibitor or ARB if unable to afford or tolerate ARNI. \*\*Also known as mineralocorticoid receptor antagonist (MRA). †Dapagliflozin and empagliflozin were studied at 10 mg daily.

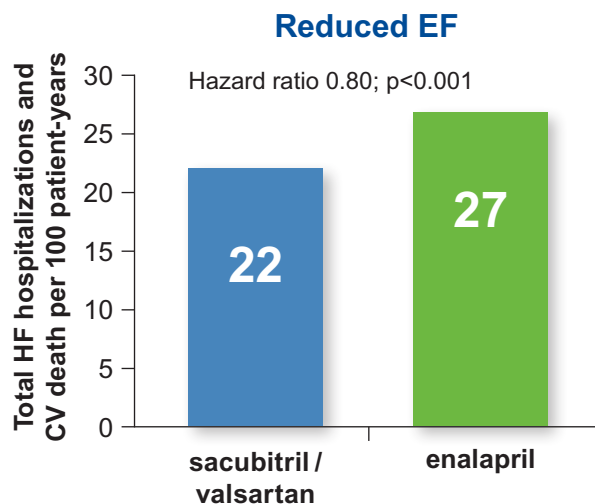
## Achieving optimal benefit

- Titrate ACE inhibitors, ARBs, ARNI, and beta blockers to maximally tolerated doses to achieve the greatest mortality benefit.<sup>11,12</sup> Even a low dose of these drugs is better than no dose.
- Additional drug therapies for HFrEF can reduce hospitalization in selected patients:
  - Hydralazine plus isosorbide for Black patients<sup>13</sup>
  - Ivabradine (Corlanor) for patients on maximally tolerated beta-blockers with heart rate > 70<sup>14</sup>
  - Vericiguat (Verquvo) for patients on outpatient IV diuretics or after HF hospitalization<sup>15</sup>
  - Digoxin if other options insufficient

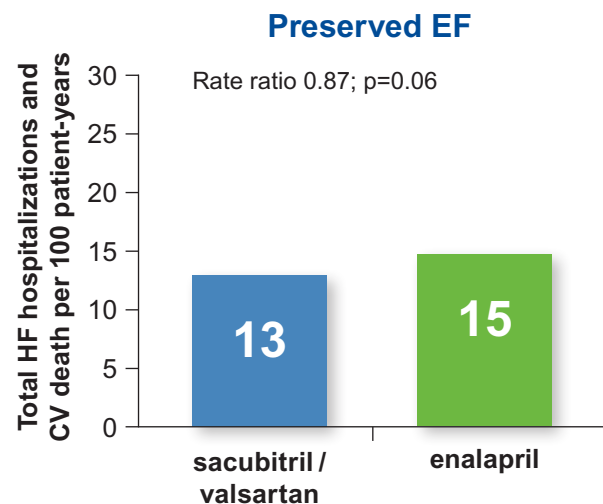
# ARNI and SGLT-2 inhibitors benefit both HFrEF and HFpEF

The ARNI sacubitril/valsartan (Entresto) should be a first-line treatment in most patients with symptomatic HF.

**FIGURE 5.** In PARADIGM-HF, sacubitril/valsartan significantly reduced mortality and HF hospitalization.<sup>16</sup>

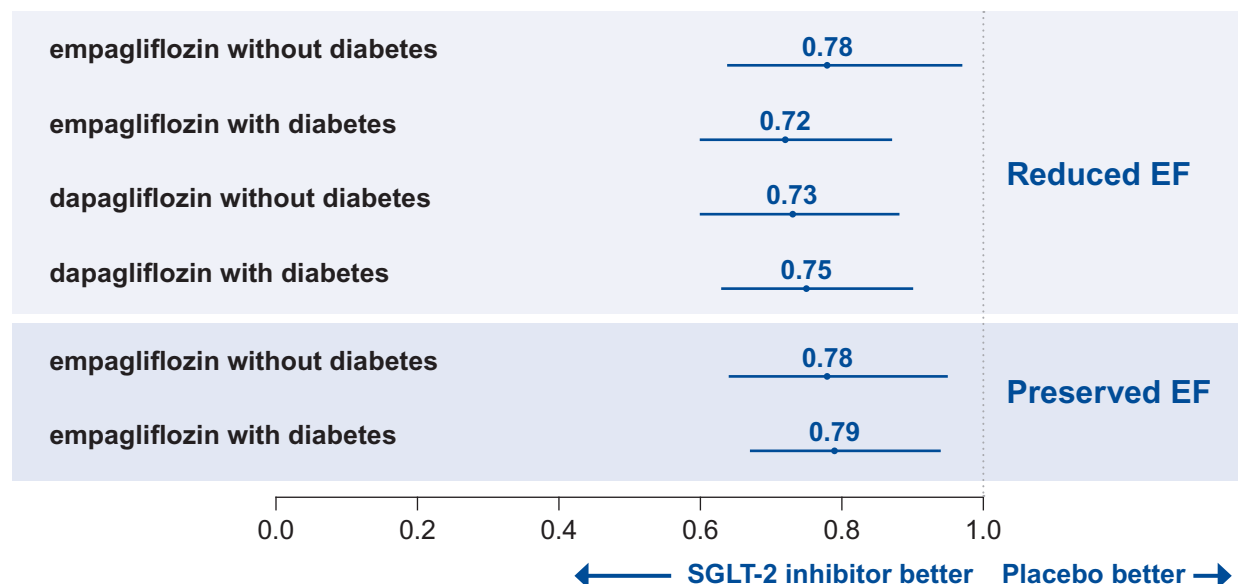


**FIGURE 6.** In PARAGON-HF, sacubitril/valsartan showed a borderline benefit in HF hospitalization and mortality.<sup>17</sup>



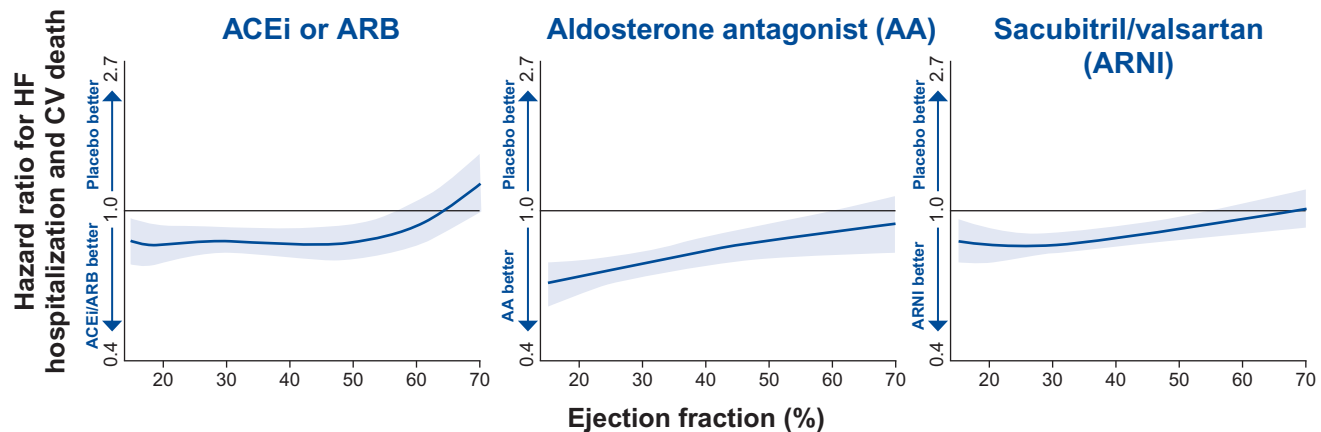
Sodium-glucose cotransporter-2 (SGLT-2) inhibitors provide benefit for HFrEF and HFpEF, even in patients without diabetes.

**FIGURE 7.** Dapagliflozin (Farxiga) and empagliflozin (Jardiance) reduce HF hospitalization and CV death in patients with HFrEF and HFpEF even in the absence of diabetes.<sup>18,19</sup>



# Patients with EF > 40% can benefit from three of the four pillars

**FIGURE 8.** Reductions in HF hospitalizations and CV death occur more consistently in patients with lower EF, but medications can also offer benefits for some patients with EF > 40%.<sup>20</sup>



Source: the CHARM program,<sup>21</sup> TOPCAT,<sup>22</sup> PARADIGM-HF<sup>16</sup> and PARAGON-HF.<sup>17</sup>  
ACE inhibitors and ARBs have similar benefits in HF outcomes.

Empagliflozin reduced HF hospitalization and death in patients with an EF < 60%.<sup>19</sup>  
Beta-blockers have not been found to reduce HF hospitalizations or mortality in patients with HFpEF.<sup>23</sup>

These data suggest that patients with mid-range EF (41-49%) should receive the same medical management as patients with reduced EF ( $\leq 40\%$ ).

## Don't forget about exercise

Frail older adults with acute decompensated heart failure benefited from a tailored exercise program three times a week (vs. usual care).<sup>24</sup>



**physical function**  
**quality of life**

The benefits occurred regardless of EF.

# Effect on HF outcomes varies by medication

**TABLE 2. Evidence summary for pharmacologic treatment of HF**

Medication	Efficacy		Target dose	Monitor
	rEF*	pEF**		
OR <b>ARNI</b> Angiotensin receptor/ neprilysin inhibitor (sacubitril/valsartan)			highest tolerated dose while maintaining adequate BP	serum potassium; renal function
			highest tolerated dose while maintaining adequate BP	serum potassium; renal function
<b>ARB or ACE inhibitor</b>			highest tolerated dose while maintaining adequate BP	serum potassium; renal function
<b>beta blocker</b> (bisoprolol, carvedilol, metoprolol XL)			highest dose tolerated for heart rate and blood pressure	heart rate
<b>aldosterone antagonist</b> (spironolactone, eplerenone)			highest tolerated dose	serum potassium; renal function
<b>SGLT-2 inhibitor</b> (dapagliflozin, empagliflozin)			10 mg daily, no dose titration	renal function; urogenital infection
<b>diuretic</b> (bumetanide, furosemide, torsemide)			as needed for symptom control	volume status; serum electrolytes; renal function
<b>hydralazine/ isosorbide dinitrate</b> <sup>†</sup>		—	highest tolerated dose while maintaining adequate BP	blood pressure
<b>digoxin</b>		—	use lower doses in older patients	renal function; digoxin level
<b>ivabradine</b> (Corlanor)		—	highest tolerated dose for heart rate	heart rate
<b>vericiguat</b> (Verquvo)		—	titrate to a dose of 10 mg daily	blood pressure

■ Reduction in mortality and HF hospitalization; ■ Reduction in HF hospitalization; ■ No benefit; — Not studied

\*rEF = reduced EF, systolic HF; \*\*pEF = preserved EF, diastolic HF; <sup>†</sup>Mortality benefit for Black patients.

## Other treatment options for patients with HFrEF that may increase survival:

- implantable cardioverter-defibrillators (ICDs) for post-MI patients with EF < 35%<sup>25</sup>
- cardiac resynchronization therapy (CRT) for patients with prolonged QRS<sup>26</sup>



# Weigh the risks and benefits of advanced therapy, and discuss the goals of care

Options for advanced therapy include:

- continuous infusion inotropes
- left ventricular assist device
- heart transplantation

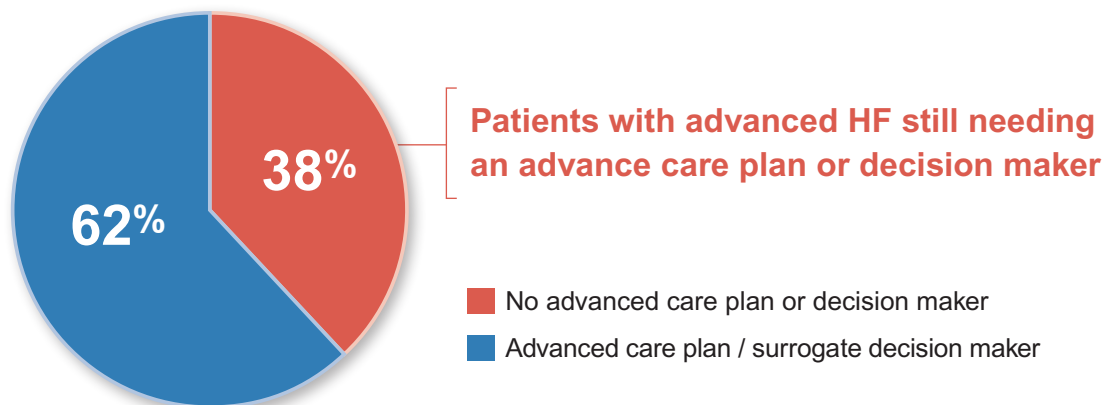
Treatment of advanced or refractory HF should focus on quality of life:

- Reduce time in the hospital.
- Review end of life goals when appropriate.
- Discuss palliative care if indicated.



Patient-centered palliative care may be the best choice for those with advanced disease.

**FIGURE 9.** In a national registry of over 120,000 patients hospitalized for heart failure, most patients discharged with advanced HF\* survived less than a year and yet many did not have an advance care plan.<sup>27</sup>

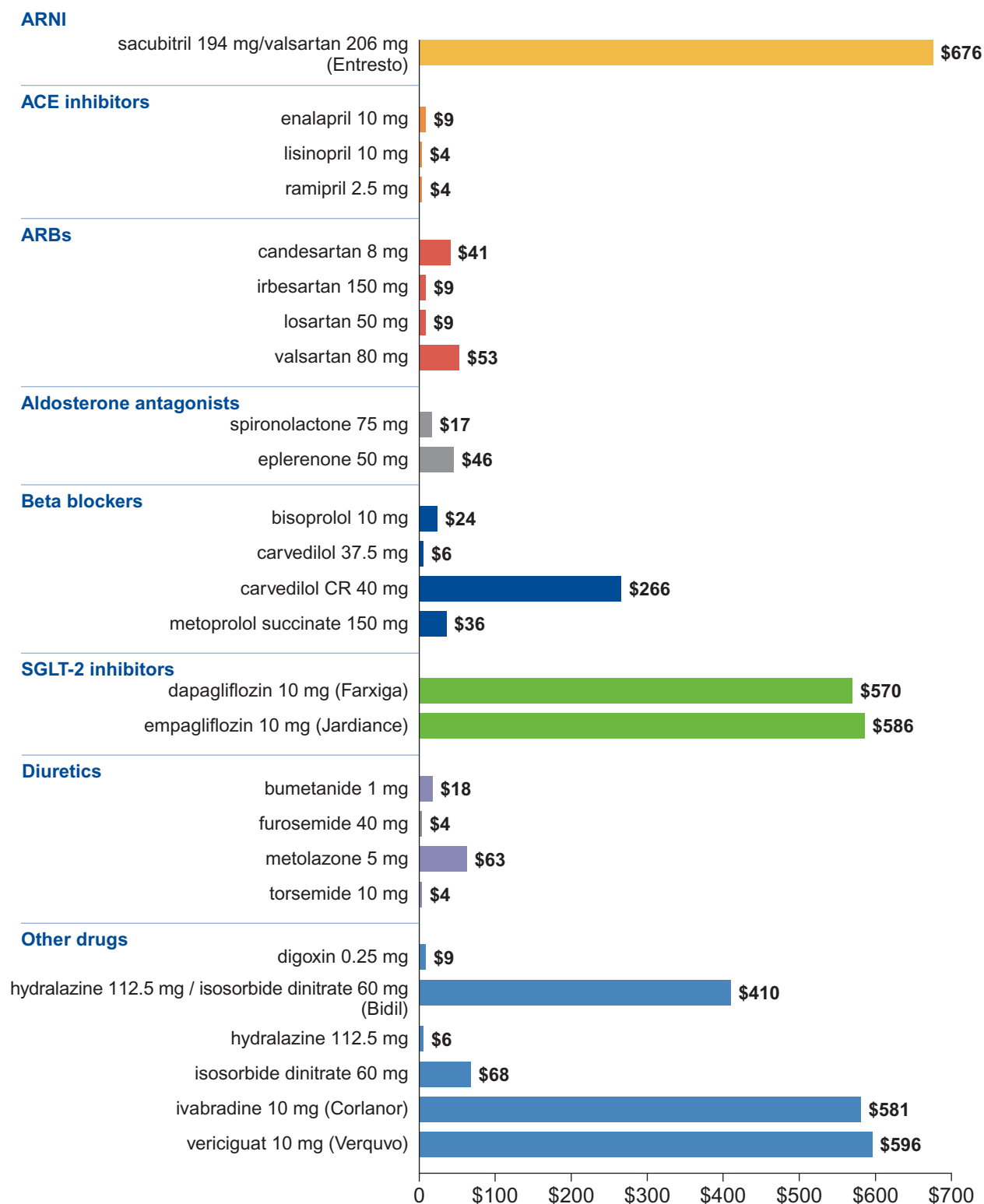


\*Advanced HF was defined here as EF  $\leq$  25% and any of the following: inpatient inotrope use, serum sodium level  $\leq$  130 mEq/L, blood urea nitrogen level  $\geq$  45 mg/dL, SBP  $\leq$  90 mm Hg, or comfort measures during hospitalization.

**For more information about discussing the goals of care in advanced disease with patients, visit [AlosaHealth.org/Serious\\_illness](https://AlosaHealth.org/Serious_illness).**

# Costs of medications vary widely

**FIGURE 10. Cost of a 30-day supply of medications used in managing heart failure**



Prices from goodrx.com, June 2021. Listed doses are based on Defined Daily Doses by the World Health Organization and should not be used for dosing in all patients. All doses shown are generics when available, unless otherwise noted. These prices are a guide; patient costs will be subject to copays, rebates, and other incentives.

# Key points

- Even in patients without symptoms, treat risk factors such as hypertension, diabetes, and atrial fibrillation to forestall the development of heart failure.
- In patients with symptomatic HF with **reduced** ejection fraction ( $\leq 40\%$ ), initiate an angiotensin system blocker (e.g., ARNI, ACE inhibitor, ARB), a beta-blocker, and an aldosterone antagonist, titrated to maximally tolerated doses, and an SGLT-2 inhibitor.
- In patients with HF with **preserved** EF, SGLT-2 inhibitors improve outcomes. An angiotensin system blocker or aldosterone antagonist may help depending on the EF.
- Patients with mildly reduced EF (40-49%) should be treated as HFrEF.
- Discuss the goals of care and advance directives for patients with advanced or refractory HF.

**Visit [AlosaHealth.org/HeartFailure](https://AlosaHealth.org/HeartFailure)**  
for links to a comprehensive evidence document and other resources.

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## About this publication

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**These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at [AlosaHealth.org](https://AlosaHealth.org).**

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