

Worsening Heart Failure: A Growing Public Health Epidemic

the facts

Heart failure is a chronic, progressive condition that occurs when the heart muscle is unable to pump enough oxygen-rich blood to the body's cells and organs.¹ The definition of **"worsening heart failure"** (WHF) is evolving. Instead of an in-hospital and clinical trial-based definition, it's now based on deterioration of HF signs and symptoms after a period of stability that requires escalation of therapy or development of breakthrough symptoms despite maximally tolerated guideline-directed therapy (GDMT).^{2,3}

Over time, the heart tries to compensate by stretching, enlarging and pumping faster to keep up with the body's demands, and becomes weakened as a result. Because this can occur without the patient recognizing any symptoms, people with heart failure may go undiagnosed for years.¹

HEART FAILURE WITH REDUCED EJECTION FRACTION (HFrEF)

Ejection fraction (EF) is a percentage measurement of how much blood the left ventricle pumps out of the heart with each contraction. A healthy heart has an ejection fraction between 50–70%, but someone with HFrEF has an ejection fraction of 40% or less.⁴

On average, ~50% of overall HF cases are classified as HFrEF.⁵ There is a large and growing heart failure patient population, with the HFrEF population expected to go from 3.1M in 2020, to 4.0M in 2032.^{6,7}

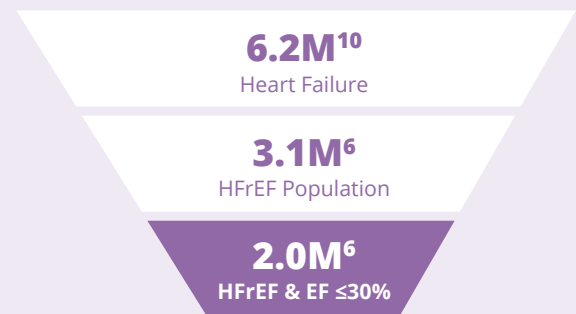


COMMON SYMPTOMS OF WHF⁹

- Shortness of breath and/or difficulty breathing during daily activities or even when lying down
- Weight gain
- "Edema" or swelling, usually in the feet, legs, ankles, or stomach
- Fatigue

ALARMING STATISTICS

Prevalence in Adults (18+, USA)
2020 Estimates



Between 2025 and 2060, prevalence of HF is expected to reach

13 million¹¹



Heart failure complications hospitalize **more Americans per year than all cancers combined**^{12, 13, 14}



Hospitalizations and rehospitalizations for heart failure patients remain high, with each additional hospitalization associated with an **increased risk of death**^{15, 16, 17}



of heart failure patients die within 5 years of diagnosis¹⁸

BURDEN OF HEART FAILURE



Financial

- The average cost for each heart failure-related hospital stay in the US is \$17k.¹⁹
- 56% of patients are re-hospitalized within 30 days of a WHF event.²⁰
- The total cost of care is expected to increase to \$69.7 billion by 2030.¹⁹
- Patients and caregivers alike experience added financial hardship due to early retirement or reduced employment hours.²¹



Physical

- Everyday activities, like walking to the mailbox, cleaning one's home, climbing stairs and participating in social activities are difficult — often leading to a poorer quality of life.²²



Caregiver

Living with HF is a “shared experience” for patients, caregivers and loved ones. Many caregivers report social isolation, anxiety, exhaustion, and fearfulness.²³



Mental

- WHF patients often feel depression and sadness, isolation, fear of dying and anxiety related to their condition.²²
- In some patients, mental health challenges can lead to further isolation from family and loved ones, missed doctor's appointments and undertreatment.²³



Comorbidities

- More than half of patients with HF have coexisting conditions such as obesity, chronic kidney disease, diabetes mellitus, hypertension and atrial fibrillation.^{24, 25}
 - 85% of HFrEF patients may be prescribed 5-14 medications.

RAASi/ARNI

Beta blocker

MRA

SGLT2i

4 PILLARS OF GDMT

TREATMENT OPTIONS

Heart failure patients may need multiple medications to treat different symptoms or contributing factors.²⁶

Recent research suggests that most patients with newly diagnosed HFrEF are treated with GDMT which includes angiotensin receptor neprilysin inhibitors (ARNIs), angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2).²⁷

Many HFrEF patients continue to worsen despite GDMT, and add-ons often result in tolerability issues.²⁸



OUTLOOK

While the term “heart *failure*” makes it sound like the heart is no longer working at all and there's nothing that can be done, what it actually means is that the heart isn't functioning as well as it should.

New and effective treatments are needed to get to the heart of the problem: enhancing cardiac performance, reducing clinical events, and improving the quality of life for this growing patient population and their families.

- ¹ American Heart Association. What is Heart Failure? May 31, 2017; Available from: <https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure>. Accessed September 2022.
- ² Greene SJ, et al. *Circ Heart Fail*. 2020;13:e007132. doi:10.1161/CIRCHEARTFAILURE.120.007132.
- ³ Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in *Circulation*. 2022 May 3;145(18):e1033] [published correction appears in *Circulation*. 2022 Sep 27;146(13):e185]. *Circulation*. 2022;145(18):e895-e1032. doi:10.1161/CIR.0000000000001063.
- ⁴ American Heart Association. Ejection Fraction Heart Failure Measurement. May 31, 2017. <https://www.heart.org/en/health-topics/heart-failure/diagnosing-heart-failure/ejection-fraction-heart-failure-measurement>. Accessed Sept. 2022.
- ⁵ Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats A. Global burden of heart failure: A comprehensive and updated review of epidemiology [published online ahead of print, 2022 Feb 12]. *Cardiovasc Res*. 2022;cvac013. doi:10.1093/cvr/cvac013.
- ⁶ Dunlay SM, Roger VL, Weston SA, Jiang R, Redfield MM. Longitudinal changes in ejection fraction in heart failure patients with preserved and reduced ejection fraction. *Circ Heart Fail*. 2012;5(6):720-726. doi:10.1161/CIRCHEARTFAILURE.111.966366.
- ⁷ Taylor CJ, Ordóñez-Mena JM, Roalfe AK, et al. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study [published correction appears in *BMJ*. 2019 Oct 8;367:l5840]. *BMJ*. 2019;364:l223. Published 2019 Feb 13. doi:10.1136/bmj.l223.
- ⁸ Carnicelli AP, Clare R, Hofmann P, et al. Characteristics and Outcomes of Patients With Heart Failure With Reduced Ejection Fraction After a Recent Worsening Heart Failure Event. *J Am Heart Assoc*. 2021;10(17):e021276. doi:10.1161/JAHA.120.021276.
- ⁹ Bozkurt B, Coats AJS, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur J Heart Fail*. 2021;23(3):352-380. doi:10.1002/ejhf.2115.
- ¹⁰ Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association [published correction appears in *Circulation*. 2020 Jan 14;141(2):e33]. *Circulation*. 2019;139(10):e56-e528. doi:10.1161/CIR.0000000000000659.
- ¹¹ Mohebi R, et al. *J Am Coll Cardiol*. 2022;80:565-578.
- ¹² GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017 [published correction appears in *Lancet*. 2019 Jun 22;393(10190):e44]. *Lancet*. 2018;392(10159):1789-1858. doi:10.1016/S0140-6736(18)32279-7.
- ¹³ Savarese G, Lund LH. Global Public Health Burden of Heart Failure. *Card Fail Rev*. 2017;3(1):7-11. doi:10.15420/cfr.2016:25:2.
- ¹⁴ Mamas MA, Sperrin M, Watson MC, et al. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland. *Eur J Heart Fail*. 2017;19(9):1095-1104. doi:10.1002/ejhf.822.
- ¹⁵ Tsao CW, Aday AW, Almarazooq ZI, et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association [published correction appears in *Circulation*. 2022 Sep 6;146(10):e141]. *Circulation*. 2022;145(8):e153-e639. doi:10.1161/CIR.0000000000001052.
- ¹⁶ Salah HM, Minhas AMK, Khan MS, et al. Causes of hospitalization in the USA between 2005 and 2018. *Eur Heart J Open*. 2021;1(1):oeab001. Published 2021 Jun 15. doi:10.1093/ehjopen/oeab001.
- ¹⁷ Harrington J, et al. Clinical Profile of Patients Hospitalized for Heart Failure with Severely Reduced Ejection Fraction: From the GWTG-HF Registry Presented at the AHA 2022.
- ¹⁸ Gaziano TA, Fonarow GC, Claggett B, et al. Cost-effectiveness Analysis of Sacubitril/Valsartan vs Enalapril in Patients With Heart Failure and Reduced Ejection Fraction. *JAMA Cardiol*. 2016;1(6):666-672. doi:10.1001/jamacardio.2016.1747.
- ¹⁹ Urbich M, Globe G, Pantiri K, et al. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014-2020). *Pharmacoeconomics*. 2020;38(11):1219-1236. doi:10.1007/s40273-020-00952-0.
- ²⁰ Butler J, Yang M, Manzi MA, et al. Clinical Course of Patients With Worsening Heart Failure With Reduced Ejection Fraction. *J Am Coll Cardiol*. 2019;73(8):935-944. doi:10.1016/j.jacc.2018.11.049.
- ²¹ Davis JD, Olsen MA, Bommarito K, et al. All-Payer Analysis of Heart Failure Hospitalization 30-Day Readmission: Comorbidities Matter. *Am J Med*. 2017;130(1):93.e9-93.e28. doi:10.1016/j.amjmed.2016.07.030.
- ²² McHorney CA, Mansukhani SG, Anatchkova M, et al. The impact of heart failure on patients and caregivers: A qualitative study. *PLoS One*. 2021;16(3):e0248240. Published 2021 Mar 11. doi:10.1371/journal.pone.0248240.
- ²³ MacMahon KMA, Lip GH. Psychological Factors in Heart Failure: A Review of the Literature. *Arch Intern Med*. 2002;162(5):509-516. doi:10.1001/archinte.162.5.509.
- ²⁴ Iyngkaran P, Majoni W, Cass A, et al. Northern Territory perspectives on heart failure with comorbidities – understanding trial validity and exploring collaborative opportunities to broaden the evidence base. *Heart Lung Circ*. 2015;24(6):536-543. doi:10.1016/j.hlc.2014.12.007.
- ²⁵ Mentz RJ, Felker GM. Noncardiac comorbidities and acute heart failure patients. *Heart Fail Clin*. 2013;9(3):359-vii. doi:10.1016/j.hfc.2013.04.003.
- ²⁶ American Heart Association. Medications Used to Treat Heart Failure. May 31, 2017. <https://www.heart.org/en/health-topics/heart-failure/treatment-options-for-heart-failure/medications-used-to-treat-heart-failure>. Accessed Sept. 2022.
- ²⁷ Dunlay SM, Killian JM, Roger VL, et al. Guideline-Directed Medical Therapy in Newly Diagnosed Heart Failure With Reduced Ejection Fraction in the Community. *J Card Fail*. 2022;28(10):1500-1508. doi:10.1016/j.cardfail.2022.07.047.
- ²⁸ Marti CN, Fonarow GC, Anker SD, et al. Medication dosing for heart failure with reduced ejection fraction - opportunities and challenges. *Eur J Heart Fail*. 2019;21(3):286-296. doi:10.1002/ejhf.1351.