HHS Public Access

Author manuscript

J Card Fail. Author manuscript; available in PMC 2023 March 01.

Published in final edited form as:

J Card Fail. 2022 March ; 28(3): 453–466. doi:10.1016/j.cardfail.2021.12.017.

Economic Issues in Heart Failure in the United States:

A Report from the Heart Failure Society of America

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Lay Summary

The cost of heart failure care is high due to cost of hospitalization and chronic treatments. Heart failure treatments vary in their benefit and cost. The cost-effectiveness of therapies can be determined by comparing the cost of treatment required to obtain a certain benefit, often defined as an increase in one year of life. This review was sponsored by the Heart Failure Society of America and describes the growing economic burden of heart failure for patients and the health care system in the United States. It also provides a summary of the cost-effectiveness of drugs, devices, diagnostic tests, hospital care, and transitions of care for patients with heart failure. Many medications that are no longer under patent are inexpensive and highly cost-effective. These include ACE inhibitors, beta-blockers and mineralocorticoid receptor antagonists. In contrast, more recently developed medications and devices, vary in cost effectiveness, and often have high out of pocket expenses for patients.

Introduction

Despite remarkable recent advances in the treatment of heart failure, the high cost of care limits delivery of effective care. The Heart Failure Society of America (HFSA) recognizes the important role of cost, cost-effectiveness, and value of diagnosis and treatment in caring for patients with heart failure. This review sponsored by HFSA describes the economic burden of heart failure, providing a summary of evidence for the cost-effectiveness of drugs, devices, diagnostic tests, hospital care, and transitions of care for patients with heart failure.

Formation of Writing Group

The Advocacy Committee of the HFSA requested its members consider developing a manuscript on economic issues in heart failure. This effort was led by the incoming committee Chair (PAH) and included committee members and non-committee members of the HFSA with expertise in this area.

Economic Burden of Heart Failure

Heart failure is a growing burden for the United States and other developed countries due in large part to the aging of their populations. The incidence is approximately 1,000,000 new patients with heart failure per year in the United States. [1] Accordingly, the cost of care for patients with heart failure is substantial. By 2030 it is estimated that over 8 million individuals in the United states will have heart failure for a prevalence rate of 1 in every 33 individuals. [2] The annual cost of caring for a patient with heart failure is near $30,000 in the United States with a wide range of estimates for other countries [3–6]. The majority of this cost is accrued for inpatient care (Figure 1).

The economic impact of heart failure is best estimated by the incremental cost due to heart failure and not the entire cost of care. The incremental cost includes both direct treatment of heart failure but also the increase in cost due to heart failure worsening other conditions. In 2012, the American Heart Association estimated the cost attributable to heart failure care to be $3,600 in direct cost and $1,700 in indirect costs per patient per year. [2] Indirect costs include cost of lost employment and are typically included in societal cost analyses. By 2030 US heart failure costs are expected to be at least 70 billion per year ($244 per every US adult) with total cost of caring for patients with heart failure reaching $160 billion. [2] Data from Canada show similar trends with estimated cost of $722 million by 2030 for a principal diagnosis of heart failure and $2.8 billion when secondary diagnoses are included. [3]

Hospitalization Trends

The greatest economic burden related to heart failure results from hospitalizations and rehospitalizations. In many analyses, 75–80% of the direct costs for heart failure are attributable to inpatient hospital stays. [1,2] In 2016, there were 809,000 hospitals discharges with a primary diagnosis of heart failure and another 2–3 million hospitalizations with heart failure as a secondary diagnosis. [1] Heart failure primarily affects older adults, is the second most common inpatient diagnosis billed to Medicare and has among one of the highest 30-day readmission rates of any other medical or surgical condition. [1,2,7] Patients with heart failure requiring inpatient admission are a highly vulnerable population and have a poor prognosis, with 1-year mortality rates exceeding 30%.[1,2,7]

From 2005–2014 hospitalizations for heart failure in the United States increased, largely driven by increased admissions for heart failure with preserved left ventricular ejection fraction. [8] However, after 2014, hospitalizations for heart failure per capita declined in the United States. [1] The reasons for this decline are unclear and likely multifactorial. Per the National Inpatient Sample, heart failure hospitalizations in the United States decreased from 1,000,000 per year in 2002 to 800,000 per year in 2016. [4] Mean hospital length of

stay also decreased by 2 days from 8.6 to 6.5 days during this time. Despite the decrease in length of stay, the cost per hospitalization (in constant dollars) has increased 1.4% per year to $19,000 in 2016 dollars.

This increase in cost per hospitalization was associated with more procedures, greater prevalence of cardiogenic shock, and renal failure requiring dialysis. [4] The reduction in length of stay was associated with fewer discharges to home (70% to 65%) and more discharges to long-term care facilities. [4] The reasons for a decline in hospitalizations is likely multifactorial. While improvements in the provision of guideline recommended care is a possible contributor, increased attention to readmission may have prompted providers to attempt outpatient management strategies for patients who would have been previously been hospitalized, though it is not clear financial penalties had a direct effect. [8]

Readmissions

The worldwide prevalence of heart failure (HF) is estimated to be 26 million and is increasing (1). In the United States, 5.7 million adults have been diagnosed with HF, with estimated annual direct costs of $39.2 billion to $60 billion (2, 3). Total HF costs in the United States are expected to exceed $70 billion by 2030 (4).

Heart failure primarily affects older persons and is the second most common inpatient diagnosis billed to Medicare (5). Patients with HF requiring inpatient admission are a vulnerable population and have a poor long-term prognosis, with a 2-year readmission-free survival rate as low as 17% (6). Risks for death and rehospitalization are accentuated immediately after inpatient discharge, with much of the economic burden in HF resulting from costly hospital readmissions. Several groups have identified transition-of-care interventions after acute hospitalization as an important area to improve patient safety and reduce HF costs (4, 7

Several groups have identified targeting reductions in readmissions after a heart failure hospitalization as an important area to reduce heart failure costs. In 2007, the Medicare Payment Advisory Commission (MedPAC) estimated that a substantial portion of Medicare beneficiaries experience a preventable hospital readmission within 30 days of discharge and recommended focusing on readmission reduction. [9] Under the 2010 Patient Protection and Affordable Care Act, the mandatory federal Hospital Readmissions Reduction Program (HRRP) was created to decrease 30-day hospital readmissions. Readmissions reporting started in 2010 and the financial penalty phase began in 2012, with hospitals with higher than expected 30-day all-cause Medicare fee-for-service (FFS) readmissions following initial hospitalization for heart failure, acute myocardial infarction, and pneumonia, penalized up to 3% of their total inpatient Medicare payments. [9] In fiscal year 2020, 83% of Medicare-participating hospitals were penalized, for a total of $563 million dollars. [9] The HRRP has altered the landscape of hospital readmissions and reimbursement within the United States, with 7.7 billion dollars in otherwise owed reimbursement to hospitals budgeted to be withheld in the first 10 years of the program.[9] As hospitals that care for heart failure patients with lower socioeconomic status tend to have higher readmission rates, irrespective of care quality, safety net and other financially vulnerable hospitals have been disproportionately impacted by these penalties.[9] While HRRP was associated with

decreases in inpatient 30-day rehospitalization rates for heart failure patients, much of the observable changes in practices after HRRP appear to have resulted from administrative upcoding and inappropriate triage, rather than improvements in transitions of care, outpatient disease management, and use of evidence-based, guideline-directed clinical practices.[9] When adjusted for coding changes observed declines were comparable to hospitals not subject to financial penalties for readmissions, suggesting either no effect or an effect independent of the penalty.[9] Of greater concern, some studies [10,11], though not all [12] have suggested that after the HRRP announcement and penalty phase, patients hospitalized with heart failure have had increases in post-discharge mortality.

Transitions of Care

While the financial penalty based policy approach appears to have been associated with unintended consequences, a number of care transition and heart failure disease management interventions have shown some success in reducing readmission, without compromising patient safety.[1,13,14] The interventions used by these programs include initiating discharge planning early in the course of hospital care, collaborating with pharmacy services in discharge planning, actively involving patients and families or caregivers in the plan of care, providing new processes and systems that ensure patient understanding of education about the plan of care before discharge from the hospital, and improving quality of care by continually monitoring adherence to national evidence-based guidelines. [14] Formal economic analysis of transitional care services after a hospitalization for heart failure, including disease management, nurse home visits and nurse case management, have suggested these are cost-effective strategies.[13] While many care coordination and transitions programs were found to decrease readmissions and costs of heart failure care, not all programs have been shown to be effective.[15]

Outpatient Trends

In contrast to the recent decline in hospitalizations, outpatient care for heart failure has increased. [1] In 2016, there were 1,932,000 office visits and 414,000 emergency department (ED) visits with a primary diagnosis of heart failure.[1] As more ambulatory care systems accept capitation or other increased risk of patient cost there will be more pressure to reduce hospitalizations and ED visits.

Disparities

Racial disparities in heart failure hospitalizations have been demonstrated with higher age-adjusted rates among black patients compared with other races. [16] Data from the Atherosclerosis Risk in Communities (ARIC) study from 2005–2014 demonstrated a higher age-adjusted rate of heart failure hospitalization for Black men (38.1 (36.6 −39.7)) per 1000 per year) than for White men (20.7 (20.0–21.3)) per 1000 per year). [16] Similar differences were noted for Black women (30.5 (29.2–31.8)) compared to White women (15.2 (14.7–15.7)). Furthermore, the trends over time indicate that rates were increasing at a faster rate over 10 years for Black men (+3.7%) and Black women (+4.3%) than for White men (+2.6%) and White women (+1.9%). [16]

Impact of COVID-19 Pandemic on Heart Failure Cost of Care

During the initial phase of the COVID-19 pandemic (through the summer of 2020) the rate of heart failure hospitalizations decreased by 30–40% in many countries. [17–20] A similar decrease in ED visits (44%) [18] was observed. The reasons for this are unclear and may be due in part to patient concerns about seeking care and hospitals being overwhelmed caring for COVID-19 patients. Further surveillance will be needed to assess whether this decline in hospitalizations is associated with an increase in mortality or will lead to a rebound in hospitalizations over time. [21]

The COVID-19 pandemic has also accelerated the use of virtual visits [22] to reduce transmission of COVID-19. These virtual visits do not incur facility or patient transportation costs though patients are often still subject to co-pays. It is likely that the use of such visits will persist when COVID-19 is no longer a significant public health threat. Yet, it is unclear whether the quality of heart failure care provided, and clinical outcomes produced are comparable to those of in-person visits. Currently, compensation for video visits remains comparable to in-person visits in the United States; though it is not clear how long this will last. Telemedicine has also been used for delivery of cardiac rehabilitation for patients for heart failure and this method is likely to continue. [23] Thus, the cost of outpatient heart failure care may have declined during the COVID-19 pandemic, with the potential impact on overall quality, costs, and outcomes requiring further study.

Measuring the Economic Value of Heart Failure Care

Value of care is often measured in units of cost per life-year gained with lower ratios indicating higher value (incremental cost-effectiveness ratio). The American College of Cardiology and American Heart Association have adopted the World Health Organization recommendation of adjusting the threshold for value using the wealth of society as measured by the Gross Domestic Product (GDP). [24] Specifically, a treatment is considered high value if the cost per life year (or quality adjusted life year) gained is less than one GDP per capita. [24] The GDP/capita in the United States in 2019 was approximately $65,000. [25] If the cost per quality adjusted life year gained is over three GDP/capita, then the value is considered poor. A similar threshold for poor value was identified using an opportunity cost approach that estimated how much individuals are willing to pay for health by comparing the amount individuals were willing to pay for private insurance against the clinical harms of not having insurance. [26] The uncertainty in the estimated cost-effectiveness varies and should be considered when evaluating the value of care. Figure 2. shows an estimate both the cost-effectiveness ratio and the uncertainty in the estimate for different heart failure care strategies.

Medications

Cost-Effectiveness of Current Heart Failure Therapies

Multiple pharmacologic therapies improve survival among patients with heart failure with reduced ejection fraction [14,27]: selected beta-blockers, angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), mineralocorticoid

receptor antagonists (MRAs), hydralazine/nitrate, sacubitril-valsartan, and sodium glucose cotransporter-2 (SGLT-2) inhibitors. [14,27] Ivabradine is an additional therapy that has been shown to improve quality of life and reduce heart failure hospitalizations. [27] Cost-effectiveness studies have evaluated the economic value of these heart failure drugs. [28–41] These studies, described in Table 1, have consistently demonstrated the high value of these therapies at conventional US cost-effectiveness thresholds.[24, 26]

Most economic analyses were performed soon after the pivotal clinical trials and therapy introduction. Due to the timing of these analyses, there are important considerations that affect their enduring applicability. First, heart failure therapies have been additive with each treatment added to prior therapies, resulting in reduction in heart failure mortality over time. [1] The economic analyses of earlier agents, such as beta-blocker or ACE-I therapy, were based on trials with higher baseline mortality and subsequently greater absolute clinical benefit than observed currently. The non-pharmaceutical costs of treating heart failure have increased over time [42] Critically important is the reduction in drug price following generic availability, particularly for beta-blockers, ACE-Is, and ARBs. A more recent economic analysis demonstrated high value at generic prices.[38]

Three major heart failure drug classes remain under patent in 2021: sacubitril-valsartan, ivabradine, and SGLT-2 inhibitors. Multiple studies have demonstrated the high value of sacubitril-valsartan.[31,36,43] Additionally, a recent analysis based on PIONEER-HF demonstrated sacubitril-valsartan was potentially cost-saving among high-risk patients hospitalized for heart failure when indirect societal costs (costs due to lost employment) were taken into account.[44] Ivabradine has one industry-sponsored cost-effectiveness study that also demonstrated high value.[33] Several SGLT-2 inhibitors are approved by the United States Food and Drug Administration (FDA) for the treatment of heart failure among patients with and without diabetes. There is a published cost-effectiveness evaluation demonstrating intermediate value with dapagliflozin using US prices.[45] Rapid analyses of the economic value of new therapies are critical to inform payer-manufacturer price negotiations and healthcare system supply for novel therapies. Likewise, there must continue to be updated analyses in the setting of changing prices and changes in heart failure epidemiology and costs.

Additional heart failure-related therapies are worth discussion. Tafamadis is an approved therapy for cardiomyopathy due to transthyretin (TTR) amyloidosis that improves survival and quality of life.[46] At its current wholesale acquisition cost of $225,000 annually, it has an incremental cost-effectiveness ratio of $880,000/quality-adjusted life year (QALY), which would be low value based on conventional US thresholds.[47] While wholesale acquisition costs are typically the best estimate of the cost of drug therapy the company may provide discounts which lower the overall cost of care. Cost-effectiveness analyses typically examine a range of drug costs that will include the cost after any discount. Patiromer acetate, a potassium binding agent, is used to enable use of ACE-I/ARB/MRA therapy among patients with hyperkalemia. A single, industry-sponsored analysis found patiromer had an incremental cost-effectiveness ratio of $52,700/QALY.[48] This study made strong assumptions regarding the overall clinical impact of patiromer based on the OPAL-HK trial, a single-arm study of patients with hyperkalemia and chronic kidney disease (including non-

heart failure patients) that demonstrated patiromer's potassium-lowering effect.[49] With limited effectiveness data, the economic value of patiromer remains uncertain.

Budget Impact of New Therapies to the System

Healthcare payers may be more concerned with a therapy's impact on its short-term total budget than on its long-term cost-effectiveness. The focus on budgetary impact is a product of multiple realities of the healthcare system. First, patients change insurances frequently. Therefore, an insurance company may be more affected by short-term costs than long-term effects. Second, insurance companies must balance their short-term budget. An increase in spending related to a given drug must be offset with other budget adjustments until premiums are adjusted. Finally, United States payers do not have accepted cost-effectiveness thresholds at which therapies are considered reasonable value for coverage. Therefore, effective therapies are "approved" but barriers are erected, such as preauthorization requirements, to limit uptake and minimize the budgetary impact.

There are limited data regarding the budgetary impact of new therapies. The Institute for Clinical and Economic Review (ICER) estimated the cost-effectiveness and budgetary impact of sacubitril-valsartan soon after its approval. It found a similar cost-effectiveness to other analyses.[50,51] Based on a high uptake of sacubitril-valsartan (75% of patients by year 5) given the substantial therapeutic benefit, it estimated a $3.0 billion annual budgetary impact. The report also calculated a value-based price benchmark. This price assumes a drug's budgetary impact should be proportional to other drugs irrespective of its relative value ($900 million per drug) or disease prevalence. Based on this analysis, sacubitril-valsartan's estimated price should be at least 9% below the wholesale acquisition cost.

Focusing on budgetary impacts biases against therapies for high-prevalence conditions. New heart failure therapies will have high budgetary impact due to heart failure's prevalence. Limiting the total spending on a drug independent of its value or disease prevalence ignores the potential to improve clinical outcomes for more patients. Coverage and pricing decisions should focus on the value of therapy rather than on the budgetary impact.

Barriers to Access

Multiple barriers have prevented optimal uptake of heart failure drugs. These include barriers erected by insurance companies – prior authorizations, copays, and deductibles – that are intended to reduce inappropriate utilization in part by forcing patients to share the cost. Unfortunately, these processes also block the adoption of high-value therapies and reduce appropriate utilization.[52]

Conceptually, prior authorization requirements restrict high-cost treatment to scenarios with evidence of clinical benefit.[53] However, the process also exacerbates the challenge of prescribing novel therapies to patients who will benefit. Prior authorization requirements are often applied indiscriminately across high-cost drugs independent of a patient's clinical characteristics. Even for those patients most likely to benefit from a therapy, gaining authorization is a time-intensive process that increases the barriers to prescribing high-value therapies. For most heart failure drugs, there is little evidence of inappropriate utilization

or indication drift, so prior authorization has minimal benefit with potential for significant harm. Prior authorization requests for heart failure drugs should be limited to scenarios where a high-cost therapy is being used for an indication with unclear benefit or where there are clinically equivalent substitutes with lower costs.

The unaffordability of heart failure therapies is a second major barrier to access. Patients are required to pay high out-of-pocket costs via copays and deductibles for many of the new cost-effective heart failure drugs. With guideline-directed heart failure management consisting of multiple therapies in addition to non-heart failure drugs, high total out-of-pocket costs can limit the affordability of heart failure treatment. Multiple studies have found high out-of-pocket costs are associated with lower rates of initial filled prescriptions and adherence to therapy.[54,55] Additionally, randomized trials have demonstrated co-pay waivers can improve therapy adherence.[56,57]

Drug cost sharing has two potential roles. First, it is an additional tool to reduce overutilization of therapies with minimal clinical benefit. Second, cost-sharing may be used for effective therapies that are low-value due to high costs, although, even in this case, cost-sharing would be expected to increase health disparities given low-income patients are less likely to be able to afford the effective therapy.

For high-value drugs, placing the burden of payment on patients may inappropriately decrease therapy rates and worsen clinical outcomes. Sacubitril-valsartan is an example of a cost-effective drug that is unaffordable for many heart failure patients, contributing to inadequate sacubitril-valsartan use and adherence, increasing heart failure morbidity and mortality.[58] Copays and deductibles should be minimal for high-value therapies like sacubitril-valsartan with current out-of-pocket costs covered by the insurance plan. [59] Prioritizing the affordability of high-value drugs is critical to maximize population-health outcomes for diseases such as heart failure.

Devices

Device use in heart failure has increased markedly in the last 40 years. Most devices are tested and approved in patients with heart failure and reduced ejection fraction, but implantable hemodynamic monitoring devices are approved for use in heart failure with preserved ejection fraction as well. The economics of devices are less favorable than those for drug therapy. However, because heart failure is, in general, a highly morbid disease with high mortality and expense, it is possible to show that expensive devices can, in certain circumstances, be economically favorable. Cost of technology implementation is highly dependent on geography and most analyses of device cost effectiveness (CE) come from the US or European perspective. Devices frequently have less robust randomized trial data prior to approval than are available for drug therapy, making uncertainty in CE model inputs higher. Finally, as time passes and/or competition develops in a device market, technology costs may drop. All of these factors increase the uncertainty in CE analyses of heart failure device therapy.

As in all economic assessments, a few factors tend to dominate economic analyses of heart failure devices. These include cost of the device, risk of death, risk of hospitalization, and magnitude of the device's effect to reduce death, hospitalization, or both. Devices with lower reliability, with significant rates of complication or lower durability, are generally associated with increased costs and this will impact economics unfavorably. Some devices may be most effective when applied to a very ill population due to the magnitude of risk and risk reduction, while others may be most effective applied to a less ill population due to a less dramatic effect that becomes economically more favorable over a longer duration of life.

Defibrillators

Nearly all defibrillator studies show a reduction in sudden cardiac death (SCD) in the implanted arm. [60.61] The overall population-benefit of the reduction, however, can be highly variable from study to study depending on background population risk. As a rule, SCD risk is highest in ischemic cardiomyopathy, and these studies tend to show clear benefit of defibrillator therapy. A paradoxical issue with implantable cardioverter defibrillators (ICD) studies, particularly primary prevention studies, is that of competing risk. In lower risk cardiomyopathy populations with reduced ejection fraction, ICD implantation leads to mortality reduction. However, as patient risk increases, competing risk of heart failure death may overwhelm device-related reductions in SCD risk and reduce value of device implantation.

Primary Prevention Defibrillators—The economic case for primary prevention ICDs is more nuanced. If one assumes a benefit of ICD therapy to prolong good quality life, the longer time horizon in primary prevention analyses (3.5 years to lifetime) tends to make these analyses more favorable. The Multicenter Automatic Defibrillator Implantation Trial (MADIT) in ischemic heart failure showed clear efficacy of ICD implantation, leading to highly cost-effective ICERs based on these criteria from $19,148 – $54,802/QALY [62–65] The case in non-ischemic cardiomyopathy depends on the level of risk reduction assumed, and here variability in randomized trial data makes modeling challenging. Using data from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), models provide an ICER in 2011 US dollars between $79,579 – $155,400/QALY.[62–64]

Secondary Prevention Defibrillators—Initial trials of ICD implantation in patients who had had an episode of ventricular arrhythmia or sudden cardiac death showed a profound benefit of the devices to reduce mortality when compared to active anti-arrhythmic therapy.[60] Implantation of an ICD for secondary prevention is a class I, level of evidence B recommendation in survivors of sudden death due to ventricular fibrillation (VF) or hemodynamically unstable sustained ventricular tachycardia (VT) [61] Nevertheless, economic models of ICD therapy show a broad range of results, even in the relatively clear-cut case of secondary prevention. A meta-analysis of the economics of implantable cardioverter defibrillators included 7 studies of CE for secondary prevention ICDs.[62] Cost-effectiveness was maximized by implanting ICDs in patients with higher risk features or lower ejection fractions. In these cases, ICERs ranged from $47,571/QALY to $142,556/QALY in 2011 US dollars.

Resynchronization Therapy

Cardiac resynchronization therapy (CRT) has been shown to reduce risk of death in patients with reduced ejection fraction and prolonged QRS duration. CRT devices cost approximately 1/3 that of defibrillators, but because they are implanted in patients with low ejection fractions, they are often combined with defibrillators, increasing cost of the therapy substantially. Economics of CRT when combined with defibrillator therapy is the subject of a recent systematic review. [66] This review concluded that CRT vs. no therapy was highly cost-effective. The value of CRT-D vs ICD alone was not as high but potentially favorable depending on a society's willingness to pay to improve outcome.

Using data from the Cardiac Resynchronization in Heart Failure (CARE-HF) trial, the cost-effectiveness of CRT was € 19,319/QALY (US $20,000-$25,000). [67] CRT has also been studied in less ill patients in the REVERSE, MADIT-CRT, and RAFT trials.[68–70] A meta-analysis examining the cost effectiveness of CRT in mild heart failure estimated a cost-effectiveness ratio of $61,700/QALY gained. [71] Recent reports examining long-term efficacy of CRT in mild heart failure have led to more favorable estimates of cost for CRT therapy, even in mild heart failure, with borderline CE when combined with defibrillator therapy if one assumes a sustained mortality reduction.

Implanted Circulatory Support Devices

Data regarding CE of durable mechanical circulatory support (MCS) devices have recently been summarized in a systematic review. [72] Implanted MCS devices increase life expectancy and quality of life in advanced heart failure patients [73–77] but are associated with obligatory upfront technology costs as well as substantial outpatient and readmission costs as well. A few studies have shown ICERs for use of MCS as a bridge to transplant near US$80,000/QALY (2017 dollars),[78–82] but others show ICERs for this strategy in excess of $100,000. [82] or even $200,000 per quality adjusted life-year gained. [83] One study suggested ICERs for long-term, or destination, MCS strategy near $200,000/QALY. [83] One analysis, however, did show a profound drop in post-discharge costs with the newest HeartMate 3 device compared to costs for the HeartWare device (no longer manufactured), driven by a reduction in rehospitalizations, suspected pump thrombosis and stroke. [77]. Ongoing assessment of costs as these technologies evolve is essential. [84,85] Cost effectiveness analyses are not currently available for short term devices utilized as acute therapy in critically ill patients with cardiogenic shock which is partially related to limited data regarding the relative efficacy of different treatment strategies in this scenario.

Cardiac Transplant

Long and colleagues compared heart transplant with destination therapy LVAD and medical therapy among transplant-eligible Inotrope-dependent Stage D heart failure. [86] They used data from ISHLT registry and the REMATCH trial and performed two analyses – a 5.6 month and 12-month waitlist for transplant. They estimated transplant led to improved outcomes and lower cost than DT-LVAD in both scenarios. Compared with medical therapy, they estimated transplant led to 4.12 additional QALYs at a lifetime incremental cost of $398,700 with a 5.6-month waitlist. This led to a cost per QALY of $96,900 of transplant relative to medical therapy with similar results with the 12-month waitlist. The primary

caveats are the basing of effectiveness estimates on observational data and the advances in transplant outcomes over time.

Mitral Valve Transcatheter Edge to Edge Repair

An analysis using the COAPT study results [87] found that transcatheter mitral valve transcatheter edge-to-edge repair (TEER) using the Mitraclip device (procedural cost $35,755) among patients with severe secondary mitral regurgitation would improve survival by 1.13 years (0.83 QALYs) and increase cost by $45,648 compared to medial therapy alone for a cost-effectiveness ratio of $55,600/QALY. [88] The benefit noted in the COAPT study has led to a 2A recommendation for TEER in the American College of Cardiology/American Heart Association clinical guidelines. [89] However, a second randomized controlled trial (MITRA-FR) using a similar population found the rate of death or unplanned hospitalization for heart failure at 1 year did not differ significantly between patients who underwent TEER and those who received medical therapy alone. [90] The uncertainty in the benefit makes it difficult to draw conclusions regarding the value of mitral valve TEER.

Diagnostic and Monitoring Tests

While clinical examination and assessment remain the gold standard for screening and diagnosing heart failure, new technological developments have added several options for clinicians managing patients with heart failure.

Brain natriuretic peptide (BNP) and N-terminal (NT) pro-BNP are now routinely used in clinical practice for the diagnosis of heart failure. The use of BNP to diagnosis of heart failure in patients with dyspnea has been shown to be cost effective.[91] More recently, there has been growing interest in using NT pro-BNP-guided management of chronic heart failure, and a 2016 Cochrane review found reduction in heart failure admissions (38% vs. 28%, relative risk 0.70, 95% confidence interval 0.61, 0.80, n=1928 patients, 10 studies, low quality of evidence) though no difference was found in any other clinical outcome. [92] Three of four studies that assessed cost found it to be cost-saving. A more recent NIH-funded RCT, GUIDE-IT, which was published after this Cochrane review, however, did not show any difference in any of the clinical or quality of life outcomes, including heart failure hospitalization.[93] Costs also averaged $5,919 higher in the NT pro-BNP guided arm (95% confidence interval -$1,795, +$13,602). Given the conflicting data, the cost-effectiveness of using natriuretic peptides for management of patients with heart failure remains uncertain.

Community screening with BNP followed by echocardiography was explored in an economic analysis.[94] Performance of BNP in asymptomatic men and women >60 years of age, followed by echocardiography, resulted in increased lifetime cost of care (176,000 US dollars for screening 1000 men, 101,000 US dollars for 1000 women) and improved outcome (7.9 quality-adjusted life years [QALYs] for 1000 men, 1.3 QALYs for 1000 women), resulting in a cost per QALY of $22,300 USD for men and $77,700 USD for women.[93]

There has also been considerable interest in using invasive hemodynamic measures to manage chronic heart failure. CardioMEMS (CardioMEMS Heart Failure System, St Jude Medical Inc, Atlanta, GA) is one such device, which has been approved by the FDA.[95] However, cost effectiveness studies show mixed results ranging from high to intermediate value. [86–98] Sandhu and colleagues found a cost of $71,462 per QALY gained.[88] The most important determinants of the device's cost-effectiveness were the durability of its effect on hospitalization and mortality over time. A recent trial found less efficacy of CardioMEMS though the population differed. [99] Thus, the cost-effectiveness of CardioMEMS is unclear and requires further study.

Cost and Value in Heart Failure Guidance Documents

As noted above, the ACC/AHA has published recommendations for including statements on cost-effectiveness and value in clinical practice guidelines and performance measure documents. [24] A recent review of 33 clinical guidance documents for heart failure found that 27 (82%) included at least one cost or value statement though most of these focused on the high economic impact of heart failure. [100] Three documents (9%) reported estimated costs of interventions and one estimated out-of-pocket cost.

Summary

The cost of heart failure care is growing due to the aging of the population and the development and new effective but costly therapies. This review has summarized the value of different care strategies and a graphical representation of these is shown in Figure 2. The review focused on high profile heart failure management strategies and published cost-effectiveness data. Thus, other important heart failure care interventions such as rehabilitation and palliative care were not included.

Given limited health care budgets, policy makers must consider the economic value that each treatment or test provides. Policies are needed to minimize out of pocket costs for all high value heart failure treatments. Such policies will directly lead to lives saved and healthier days out of hospital for patients with heart failure.

Acknowledgments

Disclosures / Conflicts of Interest

PAH: None

GCF: Consulting for Abbott, Amgen, AstraZeneca, Bayer, Cytokinetics, Edwards, Janssen, Medtronic, Merck, and Novartis.

YO: None

ATS receives research support from the National Heart, Lung, and Blood Institute (1K23HL151672–01). ATS consults for Acumen, LLC.

HJW: Advisor for Embrace Prevention Care

NKS: None

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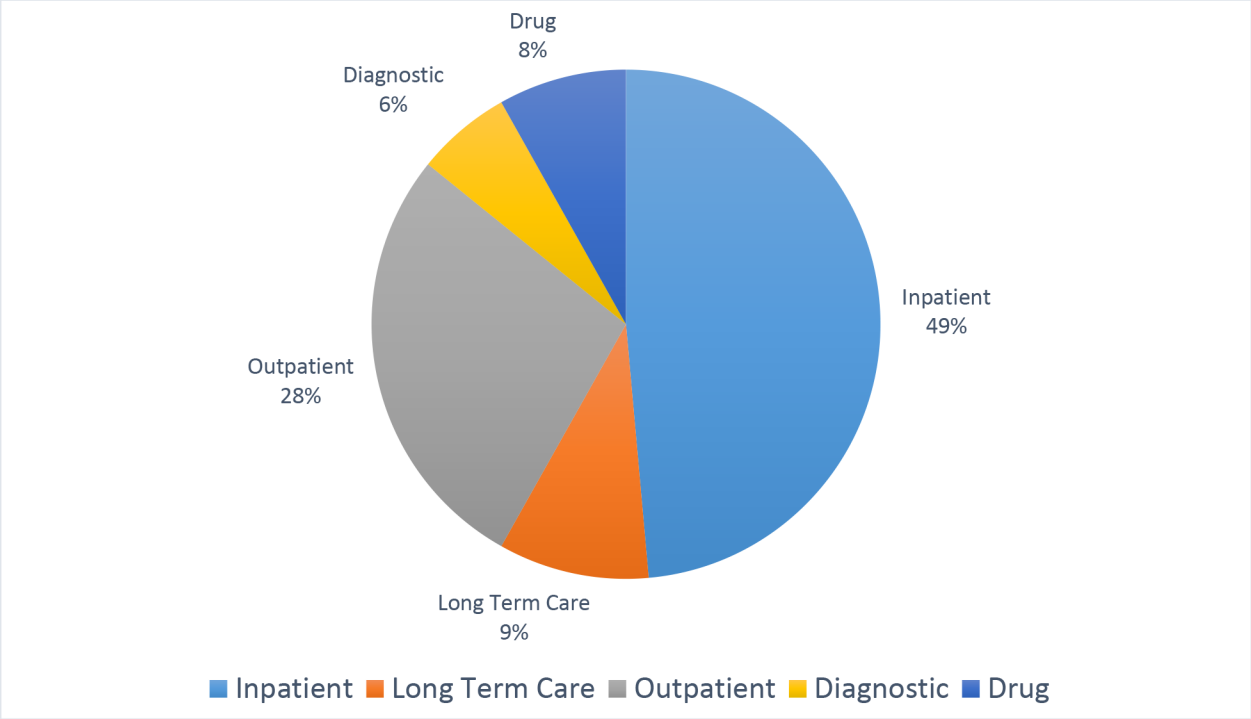

Figure 1.

The breakdown of cost of care is shown for care types (2010 resource use). [5] Since this study was performed, it is likely that care has shifted slightly to the outpatient setting.

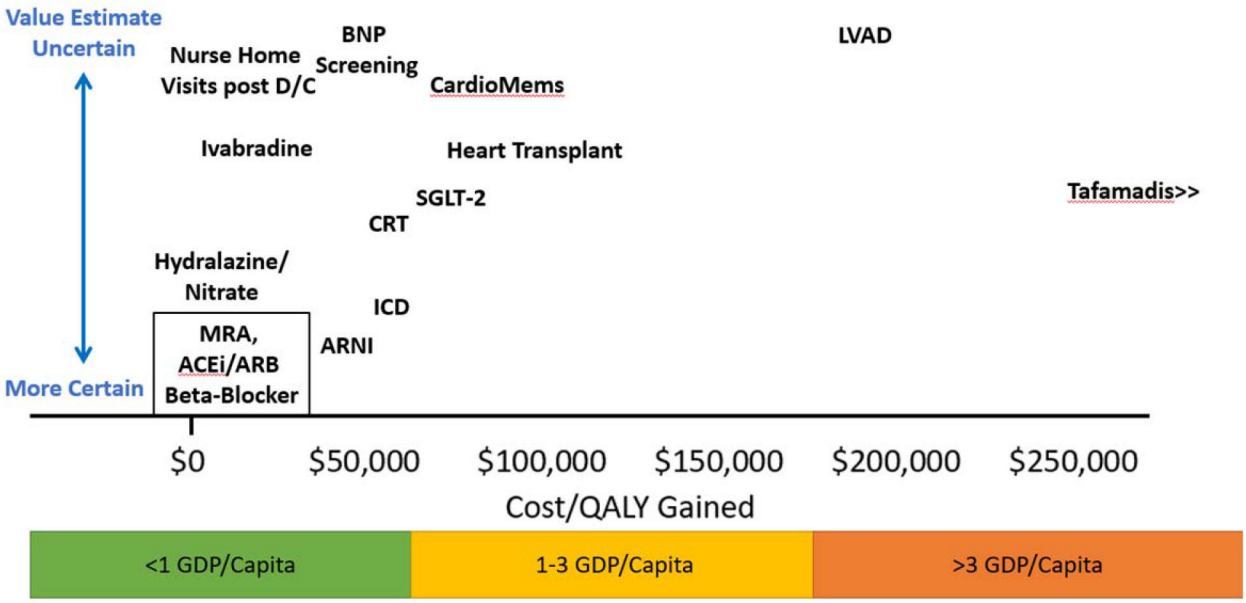

Figure 2.

Graphical representation of studies cost-effectiveness for different heart failure therapies. Value estimates are measured on the X axis in terms of cost per quality-adjusted life years gained. The Y axis shows the uncertainty in these estimates. The box outlining MRA, ACE/ARB and Beta-Blockers indicates similar value estimates and certainty of value for these groups. MRA=mineralocorticoid receptor antagonists, ACEi= angiotensin converting enzyme inhibitor, ARB=angiotensin receptor antagonist, ARNI= angiotensin receptor blocker and neprilysin inhibitor, BNP=b-type natriuretic peptide, CRT=cardiac resynchronization therapy, D/C=discharge, GDP=gross domestic product, ICD=implantable cardioverter defibrillator, LVAD=left ventricular assist device, QALY=quality adjusted life years. SGLT-2=sodium glucose co-transporter-2 inhibitors.

Table.

Selected Cost-effectiveness Studies for Heart Failure Drugs[1,2]

Drug (Estimated 2018 Cost)[3]	First Author (Year)	Industry Sponsor	CEA Cost	LY; QALY Gain	Cost Difference	ICER ($/QALY or $/LY)[4]	Comments
Beta-blockers							
Bisoprolol ($188)	Gregory (2001) [34]	N	$379	1.04; NA	$3,455	$3,336/LY	Based on CIBIS-II trial; no QALY data
Carvedilol ($55)	Delea (1999) [37]	Y	$1,096	0.79; NA	$15,735	$19,918/LY	Based on US Carvedilol Trial; no QALY data
	Gregory (2001) [34]	N	$2,000	2.40; NA	$15,656	$6,740/LY	Based on US Carvedilol Trial; no QALY data
Metoprolol Succinate ($183)	Gregory (2001) [34]	N	$612	1.06; NA	$2,613	$2,472/LY	Based on MERIT-HF and MDC Trial; no QALY data
Any ($55)[5]	Banka (2013) [38]	N	$48	0.31; 0.24	$411	$1,323/QALY	Based on MERIT-CHF trial
Angiotensin Converting Enzyme Inhibitors/Angiotensin Receptor Blockers							
Captopril ($812)	Tsevat (1995) [29]	Y	$631	NA; 0.52	$2,933	$5,600/QALY	Based on SAVE trial; results displayed for 60yo cohort
Enalapril ($192)	Paul (1994) [32]	N	$959	NA; 0.27	$2,569	$9,731/LY	Based on SOLVD and V-HeFT-II trials; only a 10-year time horizon; no QALY data
	Glick (1995) [35]	Y	$248[6]	0.30; 0.21	$25	$115/QALY	Based on SOLVD trial
Any ($40)[5]	Banka (2013) [38]	N	$48	0.15; 0.12	-$444	Dominant Strategy[7]	Based on SOLVD trial
	Shekelle (2003) [30]	N	$520[6]	0.64; 0.66	$3,718	$5,644/QALY	Based on SOLVD trial
Mineralocorticoid Receptor Antagonists							
Eplerenone ($961)	Weintraub (2005) [28]	Y	$1,138[5]	0.06–0.13; 0.04–0.09	$1,923-$2,323	$23,724-$43,301	Based on EPHESUS trial[8]
Any ($78)[5]	Banka (2013) [38]	N	$48	0.10; 0.07	$47	$501/QALY	Based on EMPHASIS-HF trial
Hydralazine-Nitrates							
Hydralazine-Nitrates ($720)	Angus (2005) [39]	Y	$1,971	0.26; NA	$10,900	$44,400/LY	Based on A-HeFT trial; assumed treatment efficacy for only a 2-year duration; no QALY data
Sacubitril-Valsartan							
Sacubitril-Valsartan ($5,315)	Sandhu (2016) [31]	N	$4,563	0.69; 0.62	$29,204	$47,053/QALY	Based on PARADIGM-HF trial
	King (2016) [43]	N	$4,560	1.08; 0.76	$38,633	$50,959/QALY	Based on PARADIGM-HF trial

	Gaziano (2016) [36]	Y	$4,500	1.43; 0.78	$35,200	$45,017/QALY	Based on PARADIGM-HF trial
	Gaziano (2020) [44]	Y	$5,628	1.51; 1.24	$27,353	$21,532/QALY	Based on PARADIGM-HF and PIONEER-HF; cost-saving when including societal indirect costs
Ivabradine							
Ivabradine ($4,706)	Kansal (2016) [33]	Y	$4,500	0.16; 0.20	$4,913	$24,920/QALY	Based on SHIFT trial; results displayed for Medicare Advantage population; only a 10-year time horizon
SGLT-2 Inhibitors							
Dapagliflozin ($5,488)	Parizo (2021) [45]	Y	$474	0.78; 0.46	$38,212	$83,650 QALY	Based on DAPA-HF trial;

[1] Abbreviations: A-HeFT: African-American Heart Failure; CIBIS-II: Cardiac Insufficiency Bisoprolol Study II; DAPA-HF: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure; EMPHASIS-HF: Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure; EPHESUS: Eplerenone Post–Acute Myocardial Infarction Heart Failure Efficacy and Survival Study; MDC: Metoprolol in Dilated Cardiomyopathy; MERIT-HF: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure; NA: not available; PARADIGM-HF: Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure; PIONEER-HF: Comparison of Sacubitril–Valsartan versus Enalapril on Effect on NT-proBNP in Patients Stabilized from an Acute Heart Failure Episode; QALY: quality-adjusted life year; SHIFT: Systolic Heart failure treatment with the If inhibitor Ivabradine Trial; SOLVD: Studies of Left Ventricular Dysfunction; V-HeFT II: Vasodilator-Heart Failure Trial II.

[2] Limited to economic evaluations that include an assessment of clinical benefit via either life-years or quality-adjusted life years and total healthcare costs. Excluded studies without a medium to long-term time horizon.

[3] Estimated cost based on Medicare Part D spending for the drug. Generic costs were utilized when available. For non-specific drugs, the drug with the lowest cost was utilized. This amount does not include proprietary rebates between patented drugs and pharmaceutical plans, which average over 20% of cost across patented drugs. For individual patients, out-of-pocket costs will vary depending on their pharmaceutical plan.

[4] When available, cost per quality-adjusted life years is preferable. For multiple studies, quality-adjusted life years was not calculated. For these studies, results were represented as $/life-year gained.

[5] Estimated cost for the lowest-cost generic in that class.

[6] Approximated based on trial drug costs and trial follow-up duration.

[7] Indicates preferable strategy given lower cost and better clinical outcomes.

[8] Modeled post-trial outcomes using three different patient cohorts leading to range of results.