The Presage ST2 Assay is an Effective Tool to Reduce 30-Day Heart Failure Hospital Readmissions

Harald Rinde MD, MBA and Lou Riceberg PhD, BioBridge Strategies, San Diego, CA

Abstract

Heart failure afflicts 23 million people worldwide and is the most rapidly growing cardiovascular disorder in the US. It is the leading cause of death in people over 65 and the third most common cause of hospitalizations in the US, with about 1.1 million discharges annually. Just as significantly, almost one quarter of patients will be rehospitalized within 30 days of discharge. With an average cost per patient for rehospitalization of $22,700, and $35,800 per patient death, this high incidence of rehospitalization and mortality has a powerful negative impact on hospitals and the healthcare system as a whole.

Importantly, newly-enacted US government regulations are forcing increased emphasis on reducing rehospitalizations for heart failure. Front and center are Centers for Medicare and Medicaid's (CMS') regulations on preventable readmissions. Effective Oct.1, 2012, hospitals with rates of rehospitalization significantly higher than expected will lose a percentage of their Medicare reimbursement across the board. In 2013, the decrease can be up to one percent of reimbursement, rising to two percent in 2014 and three percent in 2015. Indeed, as was recently reported in the news by Detroit Free Press, 2,000 hospitals nationwide will begin paying the biggest federal penalties--some as much as $1 million--because too many of their patients needed to be readmitted within 30 days of discharge for diagnoses prominently including heart failure [26].

When implemented correctly, intensive disease management programs have been demonstrated to reduce 30-day rehospitalization and mortality rates in heart failure by an average of 25%, but correct identification of those most likely to benefit from such intervention is challenging. The Presage® ST2 Assay, developed by Critical Diagnostics, was cleared by the FDA for prognosis of adverse events allowing risk stratification of heart failure patients, and thus enabling more focused advanced disease management for those patients that need them most.

To explore the impact of a strategy using ST2 to select patients for disease management programs, a decision-analytic or impact model was constructed to assess the 30-day rehospitalization, mortality, quality of life and cost outcomes as compared to the current standard of care.

The model shows that a ST2-driven disease management strategy would reduce the 30-day rehospitalization rate by 17.3%, from 24.8% to 20.5%, and would reduce the 30-day mortality rate by 17.6% from 10.2% to 8.4%. This results in a projected net cost savings of $860 per tested patient. For a typical 200-bed hospital this would mean an annual direct cost savings of about $200,000. It would also result in about 4 fewer annual deaths, or a gain of 25 quality

adjusted life years (QALYs) per year for a 200-bed hospital. If such an ST2-driven disease management program could be instituted for the 1.1 million heart failure patients admitted to hospital each year (first listed diagnosis), besides potentially saving thousands of lives and improving the lives of tens of thousands of heart failure patients, the expected annual cost savings (in addition to savings from avoidance of cuts in Medicare reimbursements) to hospitals could well exceed $1 billion, while improving overall hospital statistics for heart failure outcomes.

Our conclusion is that a ST2 post discharge disease management strategy for hospitalized heart failure patients can reduce 30-day rehospitalization and mortality, resulting in direct cost savings and improved quality scores for hospitals.

Background

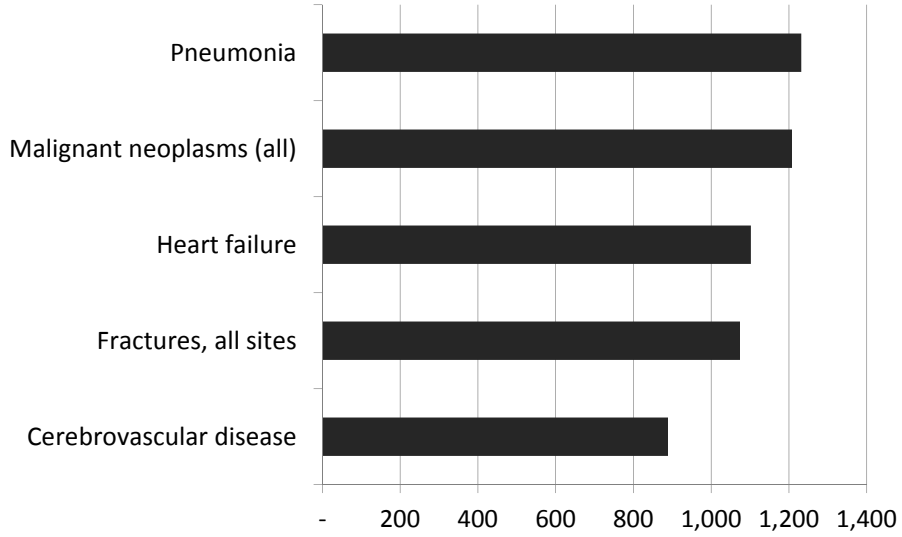
Heart failure is a chronic, progressive disease in which the ability of the heart to provide needed blood output diminishes, thus impeding the heart's ability to support the body's metabolic demands. The prevalence of heart failure is growing worldwide and causes about 280,000 deaths per year in the US [1].

When a patient is affected by heart failure, their risk for death, hospitalization or other heart failure related events is significantly higher than patients without heart failure, but a broad range of risk exists among such patients, and tools to better gauge the likelihood for adverse outcome are sought. Indeed, risk stratification in heart failure remains inadequate; clinicians continue to seek improved methods to determine patient prognosis, which might assist in the ability to better treat those patients at greatest likelihood to respond to intervention. A recent analysis, which surveyed 100 hospitals participating in the "Get With the Guidelines—Heart Failure" program for heart failure patient management showed that most current strategies for heart failure care are not associated with lower readmission rates. Despite this apparent executive-level enthusiasm for implementing processes to reduce 30-day readmission rates, our results suggest a need for better evidence and resources dedicated to effectively achieve lower readmission rates[27].

One method now available to clinicians for such assessment is the use of circulating blood biomarkers that predict risk for negative outcomes in heart failure. The Presage® ST2 Assay, developed by Critical Diagnostics, is useful for the detection of ST2, and provides powerful prognostic information in this setting. It has been used in multiple published studies, involving more than 30,000 patients. These studies have demonstrated that the level of ST2 in blood can help a physician better predict a patient's prognosis and thus make better patient management decisions than solely employing clinical parameters and existing laboratory assays.

About 5.7 million people in the United States have heart failure. Each year 1.1 million patients are hospitalized for heart failure, making it is the third most common case of hospitalization in the US (Figure 1)[1,2,25] . For perspective, this means that a typical 200-bed hospital has 234 heart failure hospitalizations per year.

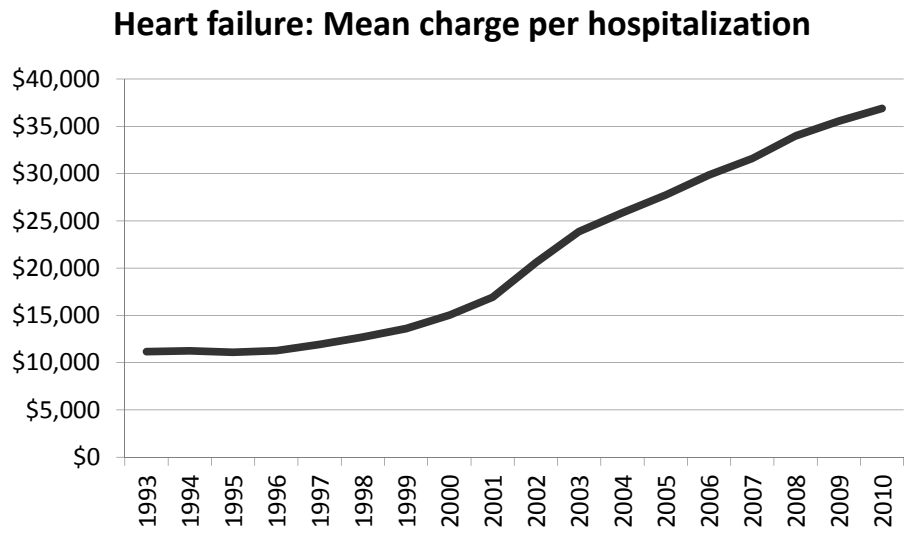
Figure 1. Heart Failure is the Third Most Common Cause of Hospitalization in the US [25]



Additionally, 670,000 heart failure patients are seen in the emergency room and heart failure results in 3.3 million doctor office visits annually [1].

The key driver of direct medical cost for heart failure is hospitalization, which costs about $36 billion in 2010, up from about $15 billion in 2000. The cost per heart failure hospitalization has steadily increased over the last 10 years from about $15,000 in 2000 to $37,000 in 2010 as illustrated in Figure 2 [2].

Figure 2. Cost per Heart Failure Hospitalization



*Mean charge per hospitalization, CCS principal diagnosis category 108, Congestive heart failure[2].

Further, heart failure is the most common reason for rehospitalization[3] and the heart failure rehospitalization rate has largely remained unchanged over the last decade[4]. The national average 30-day rehospitalization rate in the US is 24.8%. Annually about 275,000 patients are rehospitalized within 30 days of discharge[5]. The cost of these rehospitalizations alone is about $6 billion annually in the US.

The clinical challenge is to identify which of the 1.1 million discharged patients are at high risk of rehospitalization and/or death within 30 days of transition to outpatient care. Once these patients have been identified hospitals should focus their resources on these high need/high cost patients. Several efforts have been reported illustrating the effect of improved discharge procedures and disease management (DM) on reducing rehospitalization and mortality in patients with heart failure. Several systematic reviews and meta-analyses, have demonstrated a reduction in rehospitalization of 20% - 27% and a reduction of mortality of about 25%[6-12]. However, these programs rarely achieve a positive cost/benefit outcome as the resources are applied to all patients regardless of the anticipated benefit to that patient[13].

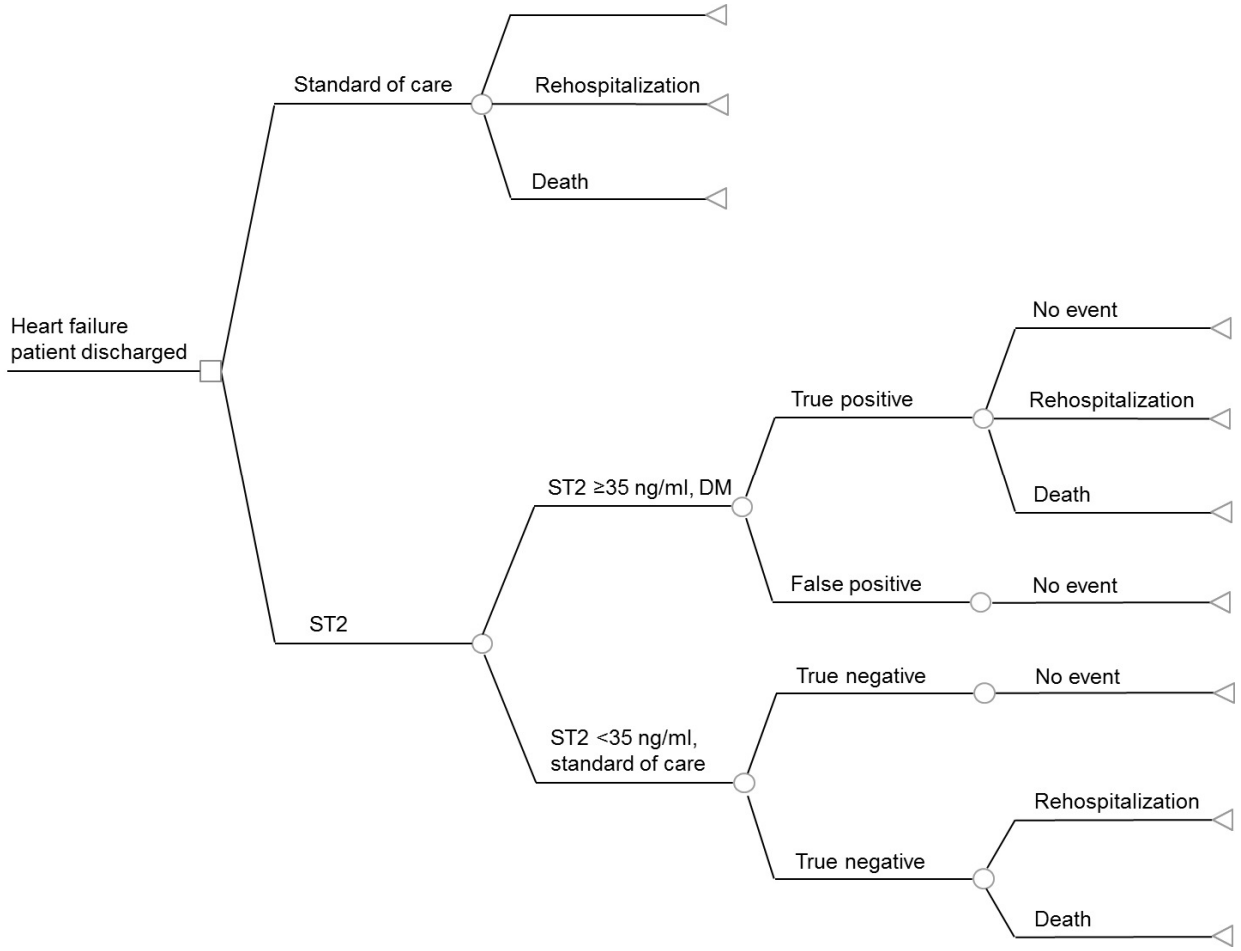
Objective

To assess the clinical and economic impact of using ST2 to identify patients at high risk of 30-day re-hospitalization or death who would be selected for post discharge advanced disease management.

Methods

To evaluate the impact of the Presage ST2 Assay as a tool to reduce 30-day rehospitalization and mortality in patients discharged from hospital care after a heart failure event, we developed a decision-analytic or impact model to explore the 30-day rehospitalization, mortality, quality of life and cost outcomes. A decision-tree model was constructed to compare two clinical scenarios. Figure 3 provides a schematic outline of the model.

Figure 3. Schematic of the Decision Tree with the two Clinical Scenarios



Clinical scenarios:

1. *Upper branch: Standard of care arm, no disease management.*
2. *Lower branch: Only patients with elevated ST2 levels (≥35 ng/ml) entered intensive patient or advanced disease management programs*. Patients with lower levels received standard of care, i.e. did not receive disease management [ST2 arm].*

* The model assumed an advanced disease management program, which included:

- Nurse-led patient education at discharge.
- Post discharge patient management by a multidisciplinary heart failure team.
- Cardiologist assessments with optional diagnostic procedures and medication review.
- Regular nurse telephone contact and home visits if deemed necessary.
- Resulting in more aggressive medication or device therapy.

The model for implementing a ST2-driven disease management strategy assumes an up-front investment in ST2 testing of $26 per test. The model also assumes that patients with ST2 levels ≥35 ng/ml will have two further tests during the 30-day period for an additional $52 per patient in this category. The hospital must also invest in the patient / disease management program. That program is assumed to cost about $1,500 per patient for the 30 days (see Table 1 for detailed breakdown). This cost accounts for a combination of cardiologist visits, nurse education session, nurse follow-up by phone and optional home visits, additional lab tests (other than ST2) and one echocardiogram or similar procedure. All, or some, of these services may be billable and could be considered revenue for the hospital thus offsetting a portion of the DM cost. However, the model includes all these services as cost. The model assumed that patients with ST2 levels ≥35 ng/ml that died only received one additional ST2 test and two weeks of disease management.

Table 1: Cost of Care Detail

	Units	Cost	Basis of calculation	Reference
Nurse days	1	$288	Based on average nurse annual salary of $69,110	16
MD hours	3	$781	Based on average cardiologist annual salary of $500,000	16
Echocardiogram	1	$290	Medicare reimbursement; CPT 93306	17
Miscellaneous lab tests (excluding ST2)		$150	Estimated	
Total cost		**$1,509**		

The model simulated a cohort of patients with a mean age of 64 over the 30-day period post heart failure hospital discharge. During that period the model assumed the US national means of 10.2% for 30-day mortality and 24.8% for all cause rehospitalization for patients receiving standard of care[5].

The model assumed a reduction in rehospitalization rate of 25% and a reduction in mortality rate of 25% relative to standard of care in patients undergoing intensive disease management.

The model used a quality of life adjustment factor, or health utility (see text box for explanation), of 0.70 for patients with heart failure without rehospitalization and 0.65 for rehospitalized patients[20, 21]. Life expectancy was calculated using the Seattle Heart Failure Model assuming patients with an age of 64 and NYHA Class III receiving ACE-inhibitors, beta blockers, furosemide and statins[19]. The health utility and life years were used to calculate quality adjusted life years (QALYs, see text box).

Other key inputs were cost of rehospitalization ($22,700) and death ($35,800), which are based on DRGs 292 and 291[2] (see Table 2) and cost of ST2 testing ($26 or $78). Performance characteristics of ST2 for prognosis at a cutpoint of 35 ng/ml were based on the mean of five heart failure clinical studies encompassing over 4500 patients[22,23,24]. In this analysis an ST2 below 35 pg/mL had a cumulative negative predictive value (NPV) for death or hospitalization of >95%.

A 200-bed hospital perspective was taken to illustrate impact. Model outcomes were 30-day readmissions, deaths, life years, quality adjusted life years (QALYs) and overall cost.

> A QALY is a measure of additional life-time gained by a medical intervention adjusted by the utility or quality of life of the patients. The utility is evaluated through standardized and validated questionnaires (which can be general quality of life questionnaires or tailored to specific diseases) and quantified by health utilities or quality of life indices. These range from 1, a perfect state of health, to 0, equivalent to death. QALYs are determined by multiplying the number of additional life years by the health utilities (for example, 4 years with a utility of 0.75 = 3 QALYs).

Table 2: DRG's for Heart Failure [2]

Diagnosis Related Group and name	Length of stay (mean)	Charges, $ (mean)
291. Heart failure & shock w mcc	6 days	$35,862
292. Heart failure & shock w cc	4.3 days	$22,734
293. Heart failure & shock w/o cc/mcc	3.1 days	$16,326

Results

Impact on Cost

The model calculated the initial per patient investment in ST2 testing ($47) and disease management ($697) added up to $744. The cost of hospitalizations and deaths was reduced from $9,296 to $7,691, or a saving in disease cost of $1,605 per patient. Taking all the various costs into consideration the model calculated the potential overall cost savings. Per discharged heart failure patient the overall savings was $862 for the ST2-driven disease management strategy when compared with no testing and receiving standard of care. This translates into a saving of $1,010 per hospital bed per year, or about $200,000 annual saving for a 200-bed hospital, Table 3. This is a conservative estimate as it assumes no disease management costs are billable, while in reality some or all may be considered revenue for the hospital thus offsetting a portion of the DM cost.

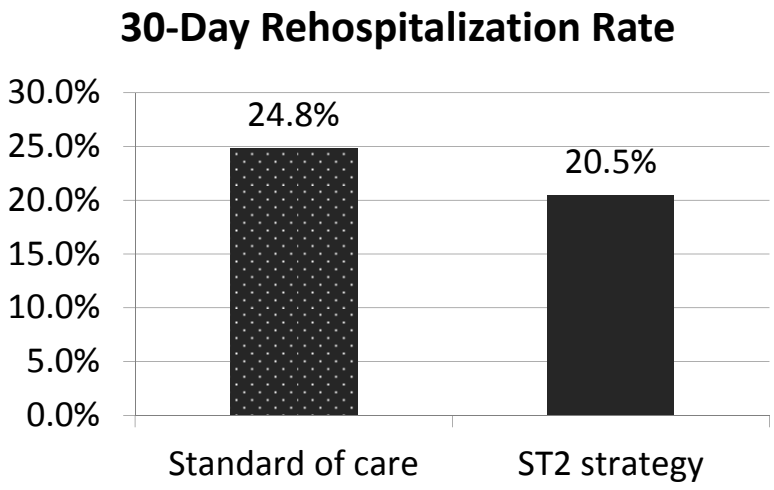
Table 3. Cost Savings from the ST2-Driven Disease Management Strategy.

	Standard of Care	ST2
Cost of testing		$47
Cost of DM		$697
Disease costs	$9,296	$7,691
Total cost	**$9,296**	**$8,434**

Impact on 30-Day Rehospitalizations

With the calculated NPV for adverse events within 30 days of >95% ST2 testing is powerful for excluding lower risk patients, and thus identifying those more likely to experience an event. Providing advanced disease management to patients at high risk of rehospitalization (ST2 levels ≥35 ng/ml) had a strong impact on reducing 30-day rehospitalizations: an ST2-driven disease management program reduced the overall 30-day rehospitalization rate from 24.8% to 20.5%, or a 17.3% reduction. Figure 4. If all high risk patients had received disease management the rehospitalization rate would have been reduced by 24.8%. The rehospitalization rate calculated by the model is a blended result of those that correctly received disease management (the true positives that should have received disease management) and those that did not receive disease management (the false negatives that should have received disease management). For a 200-bed hospital this would mean 10 fewer heart failure rehospitalizations per year.

Figure 4. Reduction in the 30-day Rehospitalization Rate

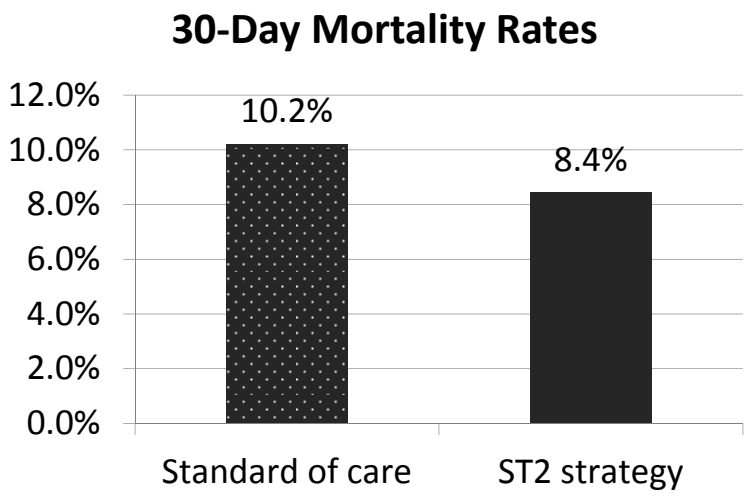


This means that a 200-bed hospital would realize a reduction of about 10 rehospitalization events, accounting for $201,000 in cost savings per year by implementing the ST2-driven disease management strategy.

Impact on 30-Day Mortality

As was shown for rehospitalization, investing in a ST2-driven disease management strategy also reduced 30-day mortality, in this case from 10.2% to 8.4% or 17.6%, Figure 5.

Figure 5. Reduction in the 30-day Mortality Rate

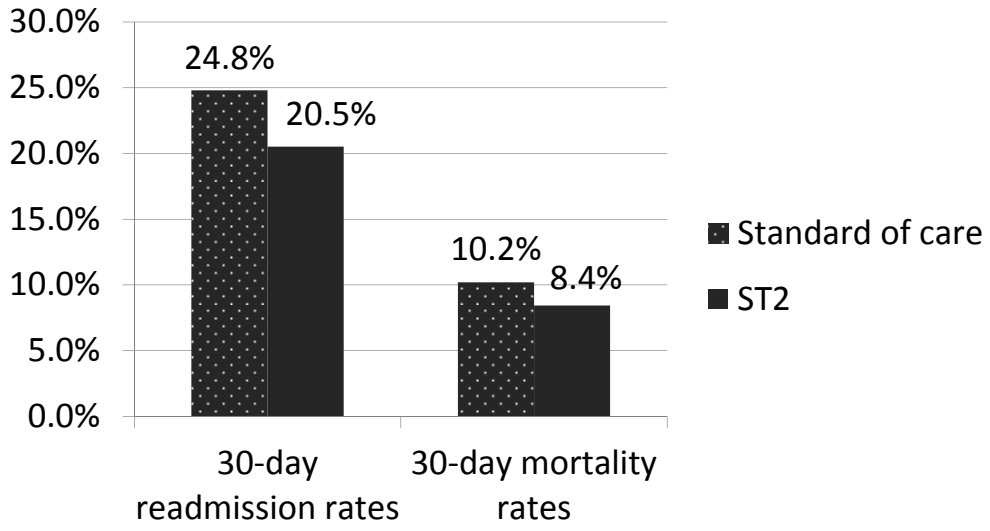


As before when applied to a 200-bed hospital this would mean four fewer deaths per year, or 25 QALYs saved, by implementing the ST2-driven disease management strategy (Figure 9).

Impact on Key Hospital Quality Metrics

Both mortality and rehospitalizations within 30 days of discharge for patients with heart failure are key hospital quality measures as discussed above. Improving these measures is important for the hospital to attract patients, medical personnel and to be in compliance with and avoid reduction in Medicare payments as a consequence of the Affordable Care Act. The ST2-driven disease management strategy substantially reduces both as can be seen in Figure 6.

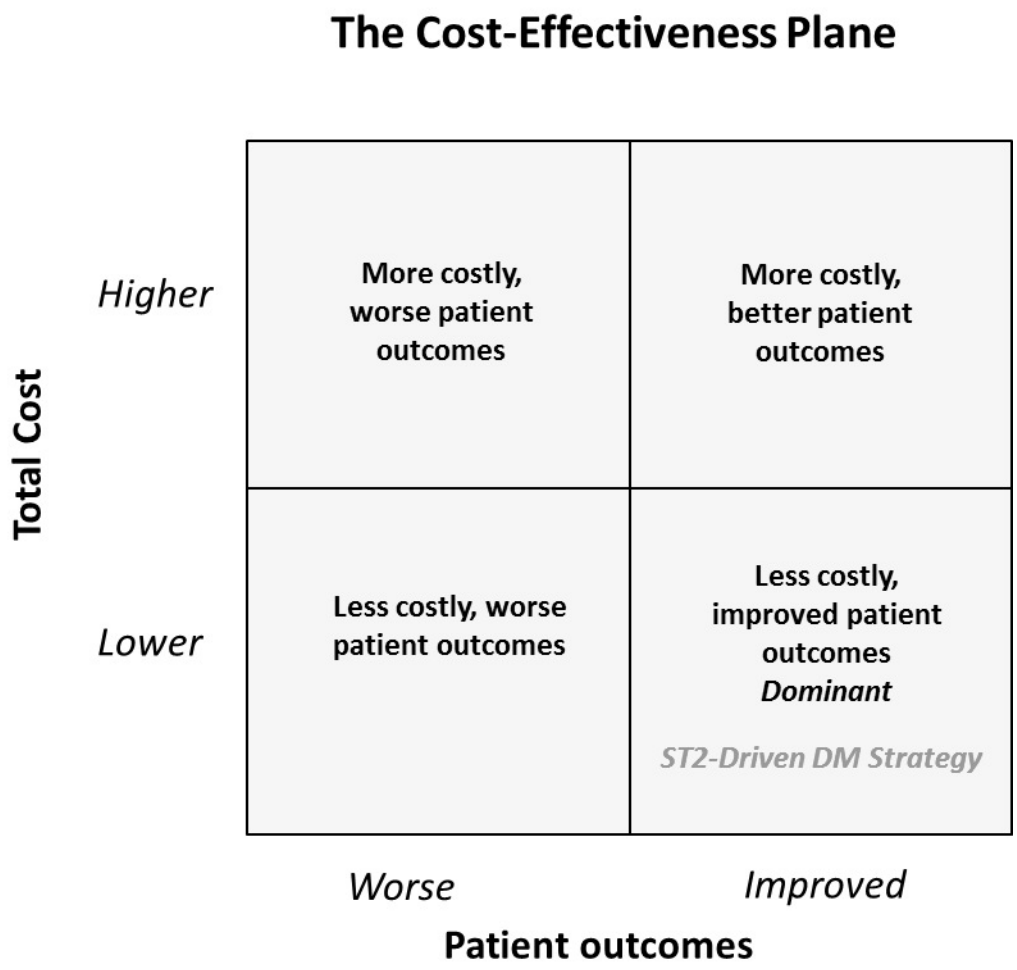
Figure 6. Reduction in Rehospitalization and Mortality from ST2-Driven Disease Management Strategy.



Conclusions

When new healthcare interventions, whether treatment, diagnostics, devices or services, undergo health economic or impact analysis as described above they will fall into one of the four quadrants of the "cost effectiveness plane". Ideally a new healthcare intervention would both improve patient outcomes (e.g. additional QALYs) and reduce cost. The ST2-driven disease management strategy falls into this desirable category, illustrated by the "cost effectiveness plane" in Figure 7.

Figure 7. The Cost-Effectiveness Plane



In summary, this analysis shows that a ST2-driven disease management strategy both reduce overall cost and provides incremental QALYs. In health economics this is referred to as being "dominant" when compared to standard of care.

- Annually there are 1.1 million hospitalizations for heart failure, with a cost of about $36 billion. 30-day rehospitalizations alone cost annually about $6 billion.
- Identifying patients that are at high risk of 30-day rehospitalization and death with ST2 enables hospitals to focus their resources on patients that can benefit most from intensive post discharge disease management.
- A ST2-driven disease management strategy has the potential to reduce the 30-day rehospitalizations and deaths by 17.3%. The strategy can save about $860 per tested patient.

- For a 200-bed hospital this means four deaths can be prevented and a saving of about $200,000 annually. Nationally, some 16,000 deaths could be avoided and savings to hospitals could top $1 billion.
- The reduction of 30-day rehospitalizations and deaths will improve these key published hospital quality metrics.

Implementing ST2 testing as part of the heart failure patient management program is a cost effective way to improve patient care while simultaneously reducing cost. For additional information about this analysis and recommended reading go to www.criticaldiagnostics.com/dmstrategy

References

1. Heart Disease and Stroke Statistics—2012 Update A Report From the American Heart Association. Circulation. 2012;125:e2-e220

2. Agency for Healthcare Research and Quality, US Department of Health & Human Services (hcupnet.ahrq.gov), 2010

3. Jencks S.F., Williams M.V., Coleman E.A Rehospitalizations among Patients in the Medicare Fee-for-Service Program, N Engl J Med 2009; 360:1418-1428

4. David C. Goodman, MD, MS, Elliott S. Fisher, MD, MPH, Chiang-Hua Chang, PhD, Stephanie R. Raymond, BA, Kristen K. Bronner, MA. After Hospitalization: A Dartmouth Atlas Report on Post-Acute Care for Medicare Beneficiaries. A Report of the Dartmouth Atlas Project. The Dartmouth Institute for Health Policy & Clinical Practice. September 28, 2011

5. U.S. Department of Health and Human Services 2012 (http://www.hospitalcompare.hhs.gov)

6. McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: A systematic review of randomized trials. *Journal of the American College of Cardiology*. 2004;44(4):810-819

7. Phillips CO, Wright SM, Kern DE, Singa RM, Shepperd S, Rubin HR. Comprehensive discharge planning with post-discharge support for older patients with congestive heart failure: A meta-analysis. *Journal of the American Medical Association*. 2004;291(11):1358-1367

8. Harris R. Review: Hospital-based case management does not reduce length of hospital stay or readmissions in adults. *Evidence Based Nursing*. 2006;9(2):54

9. Holland R, Battersby J, Harvey I, Lenaghan E, Smith J, Hay L. Systematic review of multidisciplinary interventions in heart failure. *Heart*. 2005;91(7):899-906

10. Canyon S, Meshgin N. Cardiac rehabilitation—reducing hospital readmissions through community-based programs. *Australian Family Physician*. 2008;37(7):575-577

11. Friedman SM, Mendelson DA, Kates SL, McCann RM. Geriatric co-management of proximal femur fractures: Total quality management and protocol-driven care result in better outcomes for a frail patient population. *Journal of the American Geriatrics Society*. 2008 Jul;56(7):1349-1356

12. Bellantonio S, Kenny AM, Fortinsky RH, et al. Efficacy of a geriatrics team intervention for residents in dementia-specific assisted living facilities: Effect on unanticipated transitions. *Journal of the American Geriatrics Society*. 2008;56(3):523-528

13. Kaitlyn Dmyterko . Baylor Medical Center Garland: HF Program Works, But Cost Questions Remain. September 23 2011. Cardiovascular Business

14. American Hospital Association 2012 Fast Facts on US Hospitals, AHA annual survey of hospitals in the United States 2010.

15. U.S. Bureau of Labor Statistics, Division of Occupational Employment Statistics, May 2011 (http://www.bls.gov/oes/current/oes291111.htm)

16. Cardiologist and nurse salary: http://www.theheart.org / http://www1.salary.com/Physician-Cardiology-Non-Invasive-Salary.html / http://www.healthcaresalaryonline.com/cardiologist-salary.html / U.S. Bureau of Labor Statistics

17. Echocardiogram reimbursement: http://www.medicarepaymentandreimbursement.com/2010/08/medicare-payment-for-echocardiogram-cpt.html; http://www.cms4hearts.com/billing reimbursements.asp

18. Cost of rehospitalization and death: 2010 National statistics. Outcomes for multiple specific diagnoses. http://hcupnet.ahrq.gov/HCUPnet.jsp

19. Seattle Heart Failure Model: http://depts.washington.edu/shfm/

20. Aidelsburger, Pamela, Aidelsburger, Pamela, Grabein, Kristin, Klauss, Volker, Wasem, Jürgen, Cost-effectiveness of cardiac resynchronization therapy in combination with an implantable cardioverter defibrillator (CRT-D) for the treatment of chronic heart failure from a German health care system perspective., Clin Res Cardiol, 2008-Feb; 97(2):89-97

21. Tufts Cost-Effectiveness Analysis (CEA) Registry. Mean of 52 data points from 18 publications; Patients with events: Tufts CEA Registry

22. James L. Januzzi, JR, MD, FACC, W. Frank Peacock, MD, Alan S. Maisel, MD, FACC, Claudia U. Chae, MD, MPH, FACC, Robert L. Jesse, MD, FACC, Aaron L. Baggish, MD, Michelle O'Donoghue, MD, Rahul Sakhuja, MD, Annabel A. Chen, MD, Roland R. J. van Kimmenade, MD, Kent B. Lewandrowski, MD, Donald M. Lloyd-Jones, MD, MSC, FACC, Alan H. B. Wu, PHD. Measurement of the Interleukin Family Member ST2 in Patients With Acute Dyspnea. Results From the PRIDE (Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department) Study. JACC Vol. 50, No. 7, 2007, August 14, 2007:607–13

23. Bonnie Ky, MD, MSCE; Benjamin French, PhD; Kristin McCloskey, BA; J. Eduardo Rame, MD; Erin McIntosh, BA; Puja Shahi, BA; Daniel L. Dries, MD, MPH; W.H. Wilson Tang, MD; Alan H.B. Wu, PhD; James C. Fang, MD; Rebecca Boxer, MD; Nancy K. Sweitzer, MD, PhD; Wayne C. Levy, MD; Lee R. Goldberg, MD, MPH; Mariell Jessup, MD; Thomas P. Cappola, MD, ScM. High-Sensitivity ST2 for Prediction of Adverse Outcomes in Chronic Heart Failure. Circ Heart Fail. 2011;4:180-187.

24. Data on file / publication in progress.

25. National Hospital Discharge Survey: 2006 Annual Summary, Series 13, Number 168, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Centers for Disease Control and Prevention National Center for Health Statistics, December 2010.

26. Detroit Free Press. Early patient returns trigger fines up to $1 million for 7 metro Detroit hospitals. August 27, 2012.

27. Kociol RD, Peterson ED, Hammill BG, Flynn KE, Heidenreich PA, Piña IL, Lytle BL, Albert NM, Curtis LH, Fonarow GC, Hernandez AF. National Survey of Hospital Strategies to Reduce Heart Failure Readmissions: Findings From the Get With the Guidelines-Heart Failure Registry. Circ Heart Fail. 2012 Aug 28.