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Cost-Effectiveness Of Multidisciplinary Management And Exercise Training In Heart Failure Treatment

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Introduction

As one of the major public health problems, heart failure (HF) is affecting more than 3 million patients in the United States [1]. Around 20% of all hospitalizations in populations older than 60 years of age in developed countries are caused or complicated by HF [2]. HF has been incurring above $38 billion annual health care expenditures a year, of which $23 billion is for hospital stays [3], accounting for 1-2% of total health care expenditure [4] and two third of hospitalization costs in the United States and Europe [5]. HF not only ranks the first in the most common discharge diagnoses among elderly patients, and shows extremely high readmission rates after index hospitalization, with up to 44% of patients re-hospitalized within six months of discharge [6].

In addition to pharmacologic treatments, several behavioral interventions have been receiving more attention and documented to improve quality of life and reduce hospitalization of HF patients [7]. The major interventions reported include multidisciplinary management programs (MMP) [8] and exercise training programs (ETP) [9], and both of these two methods have been proved to be effective in improving the survival of HF patients. One [10] cost-effectiveness analysis, based on a systematic literature review of clinical trials on MMP [5], estimated an incremental cost-effectiveness ratio (ICER) of $9,700 per life-year gained in MMP as compared to usual care (UC). There are two published cost-effectiveness analyses on exercise training based on two clinical trials [11, 12], respectively, and the ICERs were $1,773 and $26,462 per life-year saved, respectively. However, no comparison has been made between the cost-effectiveness of the MMP and ETP; thus it is still unclear that which one is more desirable in terms of the cost-effectiveness in HF treatment. Therefore, a cost-effectiveness analysis comparing these two interventions is needed to determine the most cost-effective intervention for HF patients.

Methods

Study population and interventions

We used published data from several literature reviews of randomized controlled trials on MMP and ETP, as shown in Table 1. The study population in the used studies was patients aged 56-80 years old with heart failure diagnosed from hospital in North America, Europe, Australia, or New Zealand. The key components of MMP included disease education for patients and continuing support, such as psychological support, dietary and social services consultation, and regular follow-ups by nurse, primary care physician, or pharmacist, or through telephone [5]. While ETP, as explained by the name itself, focused on frequent hospital-based exercise training, under the supervision of professional medical exercise trainer, as well as regular cardiopulmonary stress test during the training and basic components of MMP [13]. Therefore, ETP included exercise training in addition to the management care provided by MMP.

Structure of the model

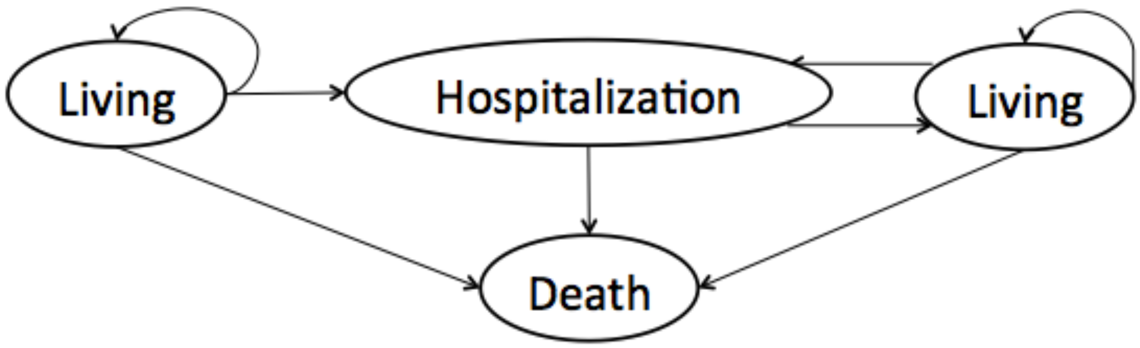


Figure 1. Markov model diagram. Patients occupy and transit among Markov states, including living, hospitalization, living after hospitalization, and death.

We developed a Markov model with eight transitional states to simulate long-term follow-ups. In this model, the patient population occupies eight states—four living states, three hospitalization states, and a death state. The living states and hospitalization states were classified by the number of previous hospitalizations, which has been proved to be a significant risk factor for HF re-hospitalization and mortality [14]. Figure 1 presented the schematic view of the Markov model.

The model starts with HF patients under a stable condition, and then moving through subsequent cycles of being alive, hospitalized, or dead. The cycle length is one month. We selected time horizon of 10 years as most of our cohort died within 8 years. At the end of each month, patients transited into the next state, according to the transitional probabilities of hospitalization and death at the current state. Patients in states other than death might continue to live, get hospitalized, or die from cardiovascular or non-cardiovascular causes at the next cycle. We assumed that the relative risks (RRs) in each intervention program compared to UC stay consistent, and the risks of hospitalization and mortality become constant after 3 times of hospitalization.

Input data

The input parameters were derived from literature reviews (Table 1). To examine the cost-effectiveness of MMP and ETP in HF, several groups of input data were needed—hospitalization rate and mortality rate in UC at a living state with no previous hospitalization, in-hospital mortality rate with no previous hospitalization, relative risks (RRs) of hospitalization and mortality in MMP and ETP comparing to the risks in UC, RRs of hospitalization and mortality with previous hospitalizations comparing to the risks without previous hospitalization, and costs of UC, MMP, and ETP. The costs of intervention programs incurred at the beginning of the follow-up, the costs of hospitalization incurred at every hospitalization, and the costs of outpatient care and wage losses were counted continuously throughout the follow-up. We assumed the costs of outpatient care, which was one of the major costs in UC, were the same in the three programs, as the the components in UC were also contained in the intervention programs. Wage loss only occurred in ETP, since patients in this program have lost working hours for exercising. A discount rate of 5% was used to calculate total costs, which were converted to the amount incurred at the beginning of follow-up. The input data used in this study came from the results of several published literature reviews, as shown in Table 1. The original hospitalization and mortality rates from the reviews were converted into monthly probabilities to perform the analyses.

	Estimate	**95% confidence**

		interval
Hospitalization rate with no previous hospitalization		
UC [10]	0.008	0.006 – 0.011
RR of hospitalization with previous hospitalizations [14]		
1*	1.28	1.23 – 1.33
2	3.32	3.21 – 3.43
Mortality rate with no previous hospitalization		
UC [10]	0.007	0.006 – 0.009
In hospital mortality		
UC [15]	0.154	0.105 – 0.202
RR of mortality with previous hospitalizations [16]		
1	1.22	1.14 – 1.30
2	1.33	1.20 – 1.47
3	1.64	1.40 – 1.91
RR of hospitalization		
MMP [5]	0.73	0.66 – 0.82
ETP [17]	0.61	0.46 – 0.80
RR of mortality		
MMP [5]	0.83	0.70 – 0.99
ETP [9]	0.64	0.40 – 1.02
Costs ($/patient) **		

MMP implementation costs [10]	826	660 – 991
ETP implementation costs [13]	2,020	1,610 – 2,428
Outpatient HF care costs for all [10]	1,871	1,497 – 2,245
Wage loss in ETP [13]	3,648	2,918 – 4,378
Hospitalization cost per stay [13]	11,413	9,130 – 13,696

Table 1. Input data: probabilities, RRs, and costs.

* Number of previous hospitalizations

** All costs are converted into 2015 U.S. dollar.

*** The total costs of interventions are the costs of intervention programs plus the cost of UC.

Cost-effectiveness analysis and sensitivity analyses

The life-years of patients and corresponding costs in each group were obtained. We calculated ICERs as cost per life-year saved. Sensitivity analyses were performed to examine the robustness of the results and address the uncertainty in the input data. We conducted one-way sensitivity analysis on the variables within clinically plausible ranges on our baseline estimates (Table 1). In the probabilistic sensitivity analysis, Monte Carlo simulation, implemented with Metropolis-Hasting algorithm [18], was used to generate 10,000 trials of follow-ups, in which each parameter was sampled from a specified distribution (beta distribution for probabilities and log-normal distribution for RRs) within its plausible range. Each trial yielded an ICER for each comparison pairs, and the distributions of the ICERs and the cost-acceptance curve from the 10,000 trials were examined at the end.

Results

Base-case analysis

	UC	MMP[1]	ETP[2]
Costs ($)	10,694	12,007	37,635
Live-year saved	6.75	7.12	7.93
Incremental costs ($)		1,313	25,628
Incremental life-year saved		0.37	0.81
Incremental C/E ($/life-year saved)		3,535	31,624

Table 2. Cost-effectiveness of MMP and ETP.

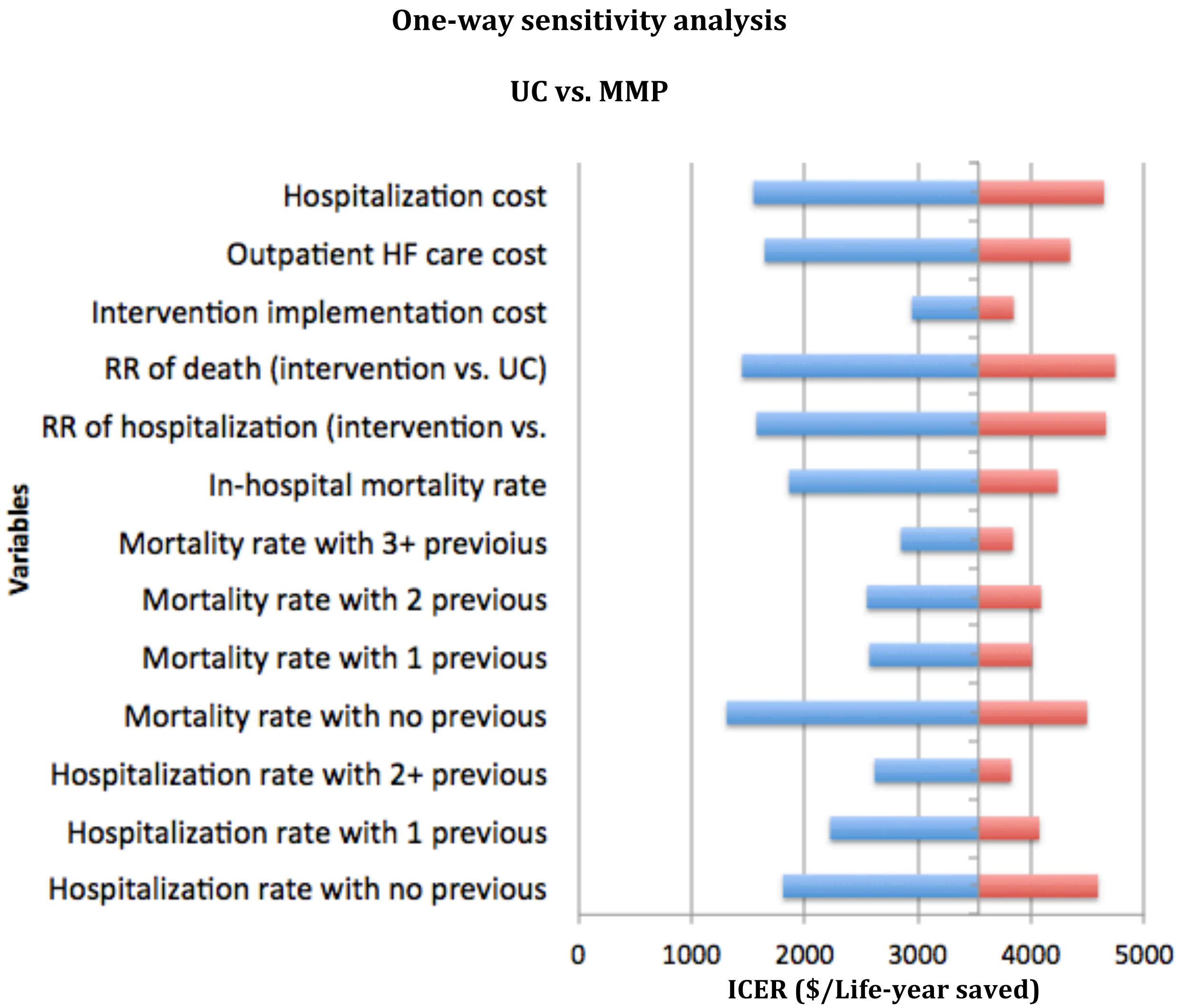
1: MMP vs. UC

2: ETP vs. MMP

Table 2 summarizes aggregate results out of a possible patient population under UC, MMP, and ETP for a 10-year follow-up period. Patients under UC lived an average of 6.75 years and accrued $10,694 in healthcare cost per patient. Under intervention programs, these same patients lived an average of 7.12 years per patient in MMP and 7.93 years per patient in ETP, and cost $12,007 per patient in MMP and $37,635 per patient in ETP. Therefore, MMP increased the patients' life expectancy by 0.37 years per patient with an additional $13,13 of healthcare costs per patient as compared to UC, and ETP achieved a

0.81-year of life-year increase for $25,628 additional cost per patient as compared to MMP. The ICERs were $3,535 per life-year saved in MMP compared to UC and $31,624 per life-year saved in ETP compared to MMP.

One-way sensitivity analysis



One-way sensitivity analysis

MMP vs. ETP

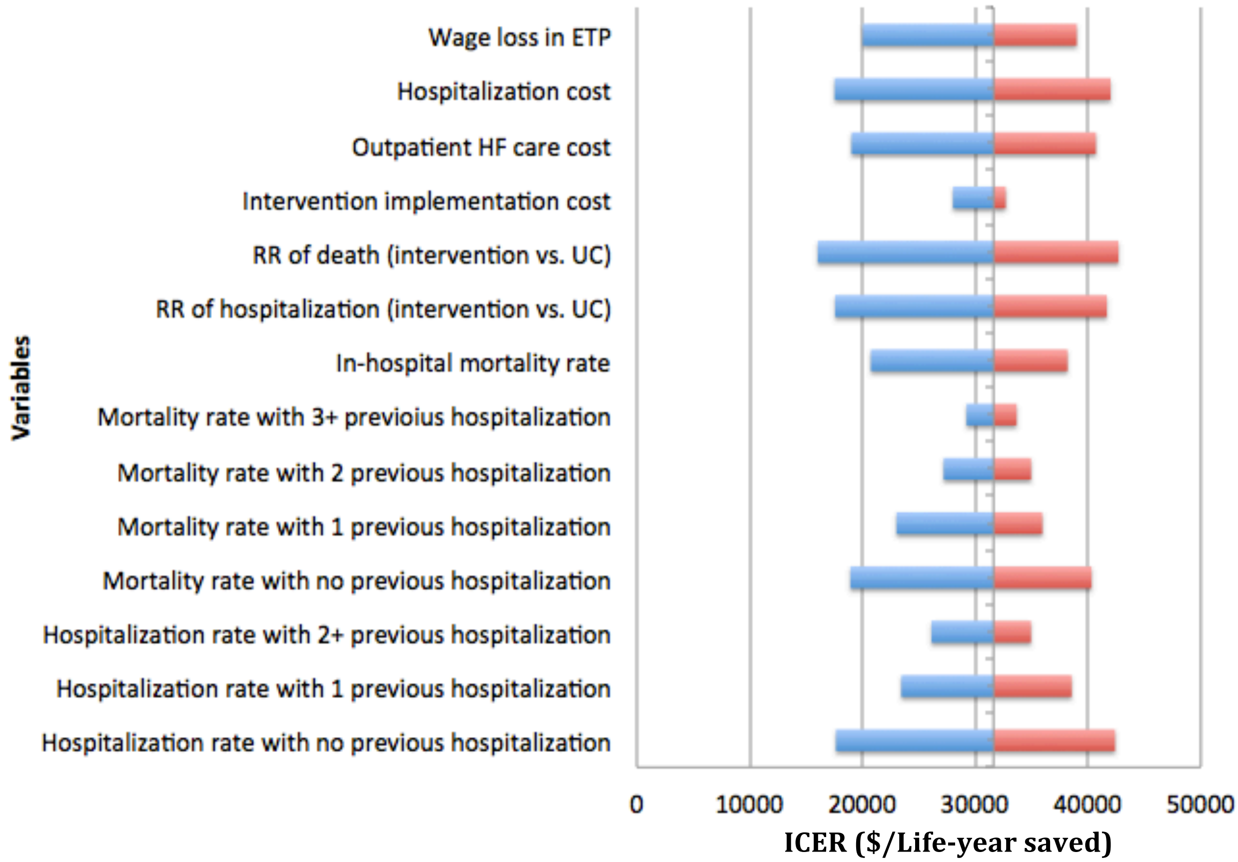


Figure 2. One-way sensitivity analysis.

Figure 2 shows the one-way sensitivity analysis, in which one of the input parameters was changed each time, within its plausible range. The ICER of MMP as compared to UC ranged from $1,307 to $4,743 per life-year saved, with the parameter change in either UC or MMP. The ICER of ETP as compared to MMP ranged from $16,043 to $42,397 per life-year saved, with the parameter change in either MMP or ETP.

Probabilistic sensitivity analysis

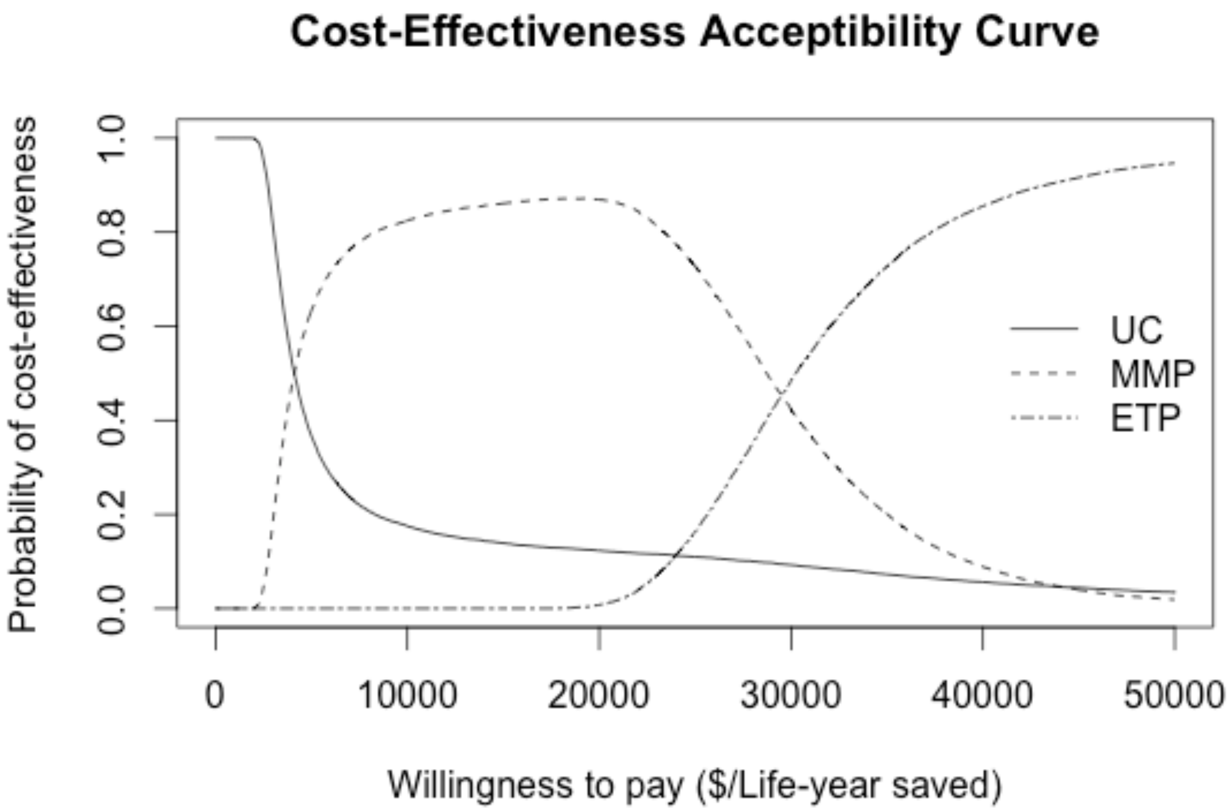


Figure 3. Cost-effectiveness acceptability curve

In the probabilistic sensitivity analysis, the median ICER of MMP comparing to UC was $3,718 per life-year saved, and the median ICER of ETP comparing to MMP was $30,006 per life-year saved. The cost-effectiveness acceptability curves (Figure 3) show that UC is the most cost-effective option when the willingness to pay is lower than $4,050 per life-year saved, MMP becomes the most cost-effective one when the budget is more than $4,015 but less than $29,697, and when the budget is more than $29,697 per life-year saved, ETP is the most cost-effective strategy.

Discussion

MMP has been a widely studied and adopted intervention program that provides HF patients continuous disease education, as well as social and psychological support. ETP serves as a more advanced intervention program that integrates the basic elements in MMP with regular exercise training to improve HF prognosis. There is evidence from multiple resources that MMP and ETP can increase the survival of HF patients in a cost-effective way by reducing hospitalization and mortality [5, 11, 19, 20]. However, the cost-effectiveness of the two intervention programs was studied individually and no direct comparison has been made between them.

This study confirmed the cost-effectiveness of MMP and ETP for treating HF patients. MMP was found to prolong the survival of HF patients and at an expected cost of $3,535 per life-year saved, and ETP further increased survival at an expected cost of $31,624 per life-year saved. With an incremental survival of 0.81 years as compared to MMP, ETP yielded much higher costs due to the wage loss, in addition to the costs of implementing the program, of patients participated in the program, which were not offset by the reduced hospital costs. Nevertheless, the results of both the two intervention programs lie within a reasonable range of cost-effectiveness in improving HF patients' survival. Furthermore, this analysis used life-year saved as the effectiveness measurement and did not incorporate quality of life, while evidences have been showing that MMP and ETP improve quality of life in HF patients; our estimates are therefore conservative in assessing the effectiveness of the two intervention programs[5, 17]. To our knowledge, this is by far the first analysis that took the two intervention programs together into consideration and assessed the cost-effectiveness acceptability of the programs, so that provided more nuanced information for deciding an optimal intervention for HF patients given a broad range of willing-to-pay threshold.

There are still some limitations in this analysis due to the data source and model assumptions. First of all, the input data of the three arms (UC, MMP, and ETP) in this analysis came from multiple literature reviews [5, 9, 10, 13, 17], therefore it is possible that the HF patients from these different sources were not exactly under the same condition when being included in the study. The hospitalization and mortality data of MMP came from the same review study [5], while the data of ETP were extracted from two studies [9, 17], since neither of the two studies alone provided complete input data for our analysis. The study populations were all elder HF patients in developed countries, but some demographic factors, such like gender, race, income, and education level, were not adjusted and might have generated differences in the outcomes among those patients. This analysis assumed that MMP and ETP applied to the same group of patients, while it is possible that some HF patients in severer conditions were not able to take ETP but could only accept MMP. The study population in ETP reviews was patients with low-to-medium risk (New York Heart Association (NYHA) class II and III) and at a median age of 60 [17], while the population in MMP studies was HF patients discharged from hospital and at a median age of 70 [5]. In that case, patients who were able to participate in ETP were healthier, younger, and at lower risks of hospitalization and death compared to those who took MMP, posing a potential bias in this comparison between MMP and ETP. These limitations might affect the generalization of the results in this analysis, and further studies are needed to generate more valid data source and more robust analytical models.

Conclusion

This cost-effectiveness analysis confirms the improvement in survival of HF patients under MMP and ETP, and compares the cost-effectiveness and acceptability of the two programs. ETP generated higher life-year saving for higher costs than MMP did. MMP was the most cost-effective way with low willing-to-pay threshold (between $4,015 and $29,697 per life-year saved), while ETP was reasonably cost-effective when the society is willing to pay more than $29,697 per life-year saved.

References

1. Ho, K.K.L., et al., *THE EPIDEMIOLOGY OF HEART-FAILURE - THE FRAMINGHAM-STUDY.* Journal of the American College of Cardiology, 1993. **22**(4): p. A6-A13.
2. Cleland, J.G.F., et al., *The EuroHeart Failure survey programme - a survey on the quality of care among patients with heart failure in Europe - Part 1: patient characteristics and diagnosis.* European Heart Journal, 2003. **24**(5): p. 442-463.
3. Oconnell, J.B. and M.R. Bristow, *ECONOMIC-IMPACT OF HEART-FAILURE IN THE UNITED-STATES - TIME FOR A DIFFERENT APPROACH.* Journal of Heart and Lung Transplantation, 1994. **13**(4): p. S107-S112.
4. Ryden-Bergsten, T. and F. Andersson, *The health care costs of heart failure in Sweden.* Journal of Internal Medicine, 1999. **246**(3): p. 275-284.
5. McAlister, F.A., et al., *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): p. 810-819.
6. Krumholz, H.M., et al., *Readmission after hospitalization for congestive heart failure among Medicare beneficiaries.* Archives of Internal Medicine, 1997. **157**(1): p. 99-104.
7. Khunti, K., et al., *Heart failure in primary care: qualitative study of current management and perceived obstacles to evidence-based diagnosis and management by general practitioners.* European Journal of Heart Failure, 2002. **4**(6): p. 771-777.
8. Holland, R., et al., *Systematic review of multidisciplinary interventions in heart failure.* Heart, 2005. **91**(7): p. 899-906.
9. Smart, N. and T.H. Marwick, *Exercise training for patients with heart failure: A systematic review of factors that improve mortality and morbidity.* American Journal of Medicine, 2004. **116**(10): p. 693-706.

10. Chan, D.C., et al., *Heart failure disease management programs: A cost-effectiveness analysis.* American Heart Journal, 2008. **155**(2): p. 332-338.
11. Belardinelli, R., et al., *Randomized, controlled trial of long-term moderate exercise training in chronic heart failure - Effects on functional capacity, quality of life, and clinical outcome.* Circulation, 1999. **99**(9): p. 1173-1182.
12. O'Connor, C.M., et al., *Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure HF-ACTION Randomized Controlled Trial.* Jama-Journal of the American Medical Association, 2009. **301**(14): p. 1439-1450.
13. Georgiou, D., et al., *Cost-effectiveness analysis of long-term moderate exercise training in chronic heart failure.* American Journal of Cardiology, 2001. **87**(8): p. 984-988.
14. Bakal, J.A., et al., *Heart Failure Re-Admission: Measuring the Ever Shortening Gap between Repeat Heart Failure Hospitalizations.* Plos One, 2014. **9**(9).
15. Panella, M., et al., *Reduced in-hospital mortality for heart failure with clinical pathways: the results of a cluster randomised controlled trial.* Quality & Safety in Health Care, 2009. **18**(5): p. 369-373.
16. Setoguchi, S., L.W. Stevenson, and S. Schneeweiss, *Repeated hospitalizations predict mortality in the community population with heart failure.* American Heart Journal, 2007. **154**(2): p. 260-266.
17. Sagar, V.A., et al., *Exercise-based rehabilitation for heart failure: systematic review and meta-analysis.* Open heart, 2015. **2**(1): p. e000163-e000163.
18. Chiang, J.W., S. Chib, and C. Narasimhan, *Markov chain Monte Carlo and models of consideration set and parameter heterogeneity.* Journal of Econometrics, 1999. **89**(1-2): p. 223-248.
19. Ahmed, A., *Quality and outcomes of heart failure care in older adults: role of multidisciplinary disease-management programs.* Journal of the American Geriatrics Society, 2002. **50**(9): p. 1590-3.
20. Davies, E.J., et al., *Exercise training for systolic heart failure: Cochrane systematic review and meta-analysis.* European Journal of Heart Failure, 2010. **12**(7): p. 706-715.