

Heart Failure (Multi-Disciplinary Community Care) Clinics Field Evaluation

THETA Cardiac Group



Contents

Executive Summary	i
Background	i
Methods	i
Results	i
Conclusions	ii
Chapter 1: Introduction	1
Background	
Research Questions	
Figure 1	
Figure 1	3
Chapter 2: An Environmental Scan of Specialized Multi-Disciplinary Heart Failure Clinics in	4
Ontario	
Objective	
Methods	
Identification of Heart Failure Clinics	
Semi-structured Interviews	
Institutional Review Board	
Results	
HF Clinic Identification	
Regional Distribution of HF Clinics	9
Clinic Characteristics	9
Access to Allied Health Professionals	9
Intensity and Complexity	9
Concept Mapping	10
Discussion	11
Table 1: Seed Heart Failure Clinics	13
Table 2: Heart Failure Disease Management Scoring Instrument (HF-DMSI)	14
Table 3: Geographic Distribution of Clinics	15
Table 4: Characteristics of 30 identified clinics	16
Table 5: Clinic Intensity and Complexity	17
Figure 1: Identification of Heart Failure Clinics through Snowball Sampling	18
Figure 2: Geographic Distribution of Heart Failure Clinics	19
Figure 3: Scores on Heart Failure Disease Management Scoring Instrument (HF-DMSI).	20

Appendix A	21
Heart Failure Clinic Stratification using Concept Mapping	21
Chapter 3: Insights into the Contemporary Management of Heart Failure in Specialized Mult	i-
Disciplinary Ambulatory Clinics	23
Objective	24
Methods	25
Clinic Selection	25
Chart Abstraction	25
Analytic Plan and Study Definitions	25
Statistical Analyses	26
Institutional Review Board	26
Results	27
Baseline Characteristics of HF patients	27
Clinic Visits and Diagnostic Tests	27
Medication Use	27
Comparison of Early vs. Recent Cohorts	28
Target Doses of ACEi/ARB and β-blockers	28
Predictors of ACEi/ARB and β-blocker use	28
Discussion	30
Table 1: Baseline Characteristics	32
Table 2: Diagnostic Test Performed over 1 year of chart abstraction	33
Table 3: Medication ever prescribed	34
Table 4: Medication- Any time during the visits at target dose of evidence-based medication (among users)	35
Table 5: Predictors of medication prescription	
Table 6: Predictors of ever achieving the target dose of medication	
Table 7: Comparison of patient characteristics between 1995-2005(early) and 2006-202 cohorts (recent)	10
Table 8: Comparison of HF management patterns between 1995-2005 and 2006-2010 cohorts	
Appendix A	
Recommended B-blockers	
Recommended ACE/ARB	
Figure 1: Patient distribution by year of first visit and HF clinics	
Tibare 1.1 attent distribution by year of first visit and fir clinics	+J

Chapter 4: Effectiveness and economic evaluation of multi-disciplinary heart failure clinics: a population based study
Objective
Methods
Research Ethics Board Approval
Data Sources
Study Design and Sample
Outcomes
Statistical Analyses
Sensitivity Analyses
Results
Study Sample50
Baseline Characteristics
Clinical Outcomes
Predictors of Improved Outcome
Economic Outcomes
Sensitivity Analyses
Discussion
Table 1: Baseline Characteristics of Matched Cohort
Table 2: Clinical and Economic Outcomes
Table 3: Clinic Level Predictors of Outcome
Figure 1: Study Outline
Figure 2
Figure 3
Appendix 1
Appendix 2: Excluded Hospitals65
Appendix 3: Economic Outcomes
Appendix 4: List of Covariates
Appendix 5: Baseline Characteristics of Unmatched Cohorts
Appendix 6: Disease management interventions in heart failure clinics* (n = 21) 71
Appendix 7: EFFECT II HF cohort: Standardized Differences of baseline covariates in original and matched sample72
Appendix 8: Landmark Analysis
Reference List
Acknowledgments

Executive Summary

Background

Multi-disciplinary heart failure (HF) clinics have been shown to improve outcomes for HF patients in randomized clinical trials. However, it is unclear if this improved efficacy translates to improved real world effectiveness or which components of care at HF clinics are related to improved outcomes.

Methods

We performed a field evaluation of existing HF clinics in Ontario. First, an environmental scan was performed to identify all HF clinics currently in operation. A semi-structured interview was conducted at each clinic to understand the scope of practise. The intensity and complexity of care offered at the identified clinics were quantified through the use of a validated instrument, and clinics were categorized as high/medium or low intensity clinics. Next, all patients discharged alive from hospital in 2006-07 with a primary diagnosis of HF were identified and classified as either HF clinic or standard care patients. Propensity score matching was performed and these two cohorts were followed until March 31st, 2010, to evaluate mortality, all-cause rehospitalisation, and HF hospitalization. Cumulative health care costs were also estimated.

Results

We identified 34 clinics in Ontario, with 143 HF physicians. The majority of HF physicians were cardiologists (81%), with 81% of the clinics based in hospitals, of which 26% were academic centers. There was substantial range in

the complexity of services offered, most notably in the intensity of education and medication management services offered.

14,468 post-discharge HF patients were identified, with 1,288 HF clinic patients. Over 3 years of follow-up, 52.1% of HF clinic patients died, compared to 54.7% of standard care patients (p-value 0.02). More HF patients were hospitalized (87.4% vs 86.6% for all-cause [p-value 0.009];58.7% vs 47.3% for HF-related [p-value <0.001). The mean cumulative cost for a HF clinic patient was \$54,311 compared to \$39,994 for a standard care patient (p value <0.001).

We found that high intensity clinics were associated with lower mortality (hazard ratio [HR] 0.7 (95% confidence interval [CI] 0.54-0.92; p-value 0.011) but higher rates of both all-cause hospitalization (HR 2.05; 95% CI 1.49-2.82; p-value <0.001) and HF hospitalization (HR 1.51; 95% CI 1.08-2.10; p-value 0.015), compared to medium or low intensity clinics. HF clinics that targeted both the patient and caregiver were associated with improved survival, as were clinics with peer support as an important component of the intervention (Table 3). More complex clinics with multiple contacts between providers and patients of significant duration had a significant reduction in mortality (HR 0.17; 95% CI 0.11-0.27; p-value < 0.0001) compared to clinics with only a single contact with little or no follow-up. A more intensive medication management program was associated with reduced all cause and HF hospitalization (HR 0.28 and HR 0.37 respectively).

Conclusions

Multi-disciplinary HF clinics improve outcomes in HF patients, with complexity of care, and intensity of medication management as key components.

Chapter 1: Introduction



Background

Heart failure (HF) is a complex, progressive syndrome characterized by abnormal heart function resulting in poor exercise tolerance, recurrent hospitalizations, and reductions in both quality of life, and survival.(1) Although tremendous progress has been made in pharmacologic and device therapy, HF patients continue to have a poor prognosis, with an annual mortality ranging from 5% to 50%.(1) The incidence of HF is projected to increase, with estimates suggesting a three-fold increase in HF hospitalizations over the next decade.(2) Alternative targeted health care delivery models have therefore been of particular interest in HF, as a means of improving both quality of life and survival.(3)

Disease management through multidisciplinary community care clinics has been shown to improve patient outcomes in different health conditions, including diabetes, chronic kidney disease, and cancer.(4;5) The potential benefits of a multi-disciplinary strategy in HF include improved utilization and compliance with evidence-based medications. In addition, this model of care may better address the complex interplay between medical, psychosocial, and behavioural factors facing these patients and their caregivers.(3) Multiple previous randomized studies and meta-analyses have evaluated the efficacy of such clinics with some suggesting a reduction in mortality.(1;3;6) However, interpreting this literature is challenging because of substantial heterogeneity in the composition of the HF clinics, the interventions they offer, and the population studied.(3)

Recently, the Medical Advisory Secretariat (MAS) conducted a systematic review of published randomized controlled trials evaluating the efficacy of specialized clinics in the management of HF patients.(7) Their findings suggested that clinics that included at a minimum, a physician and nurse with expertise in HF management, showed a relative reduction in mortality of about 30%. A subsequent economic evaluation and budget impact analysis conducted by THETA found that HF clinics appear to be a cost effective way of delivering ambulatory care to HF patients, with an incremental costeffectiveness ratio (ICER) of \$18,259/life year gained (www.theta.utoronto.ca).

An important limitation to these analyses is heterogeneity in the summary efficacy estimates from the published literature. Moreover, efficacy estimates from randomized trials with highly restrictive enrolment criteria are not necessarily reflective of clinical effectiveness in real world practise. Thus, there remains uncertainty about the true effect of HF clinics on mortality. Also, it is unclear which components of specialized HF clinics are most critical. For example, it is unknown if their beneficial effect is mediated through more aggressive medication titration, or through enriched surveillance through education programs.

Currently, specialized HF clinics do not receive specific funding from the Ontario Ministry of Health and Long Term Care (MOHLTC), the third party payer for government insured health services in the province. It is not known how widely available specialized HF

clinics are in Ontario, nor has their composition, or the services they offer, been described. It is unclear if the efficacy of HF clinics in randomized trials is generalizable to the HF clinics currently in place in Ontario.

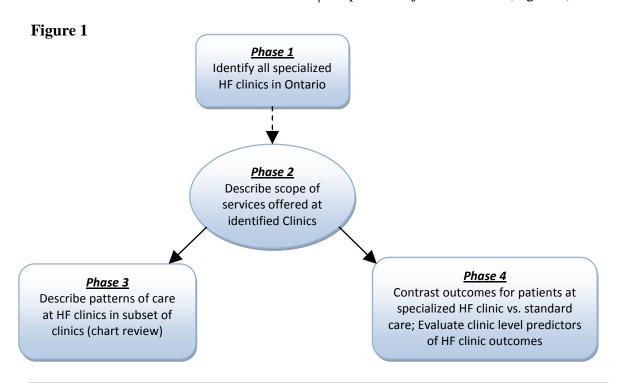
Our objective was to address these important gaps in knowledge, through a field evaluation or pragmatic trial, whereby real world practise for HF patients in Ontario is assessed. Specially, we aimed to understand the current availability of specialized HF clinics in the province, the scope of services offered, and the economic and clinical outcomes for Ontario patients treated at current specialized HF clinics, in contrast to those treated by standard care. Importantly, we sought to understand which component of the multi-disciplinary clinic was associated with improved outcomes.

Research Questions

The overall research question for this field evaluation was to understand the current service models used and related effectiveness and cost-effectiveness of HF clinics in Ontario. The specific objectives of the project were as follows:

- 1. Identify all specialized HF clinics in Ontario
- 2. Describe scope of current service models for patients in specialized HF clinics
- 3. Understand practise patterns for patients in a subset of identified clinics
- 4. Assess the clinical effectiveness and cost-effectiveness of HF clinics in Ontario
- 5. Understand clinic level characteristics associated with HF clinic outcomes

The study itself was arranged in the following framework, reflecting the specific objectives above (Figure 1).



Chapter 2: An Environmental Scan of Specialized Multi-Disciplinary Heart Failure Clinics in Ontario



Objective

Identify all HF clinics in Ontario and describe service models, and intensity/complexity of services offered.

Methods

Identification of Heart Failure Clinics

For the purpose of this project, a specialized HF clinic was defined as a clinic that consists *at a minimum* of a physician (family physician/internists/cardiologists) and a nurse, one of whom has specialized training/interest in HF. This definition is consistent with that used in recent systematic reviews of HF clinics.(7)

Currently, it is not known how many specialized HF clinics, based on the above definition, are present in Ontario. Therefore, we utilized three approaches to identify clinics. First, all hospitals listed on the MOHLTC site were systematically contacted in order to identify any HF clinics. As well, notices were posted in the Cardiac Care Network (CCN) forum asking clinics to identify themselves. Finally, we used an approach often used in qualitative or mixed methods research studies, typically when evaluating 'hidden populations'.(8)

A hidden population is one in which a sample frame (i.e. a list of all the members of the population) cannot be constructed, thereby preventing probability sampling.(8) An alternative to probability sampling that does not require a sampling frame is chain-referral sampling, whereby new members are selected from the social network of existing members of the sample.(8) An efficient method to penetrate hidden populations is to use a variant of chain-referral sampling termed snow-balling sampling.(8)

In this method, first a number of seeds are selected.(8) These seeds are members of the hidden population that

have been identified. The seeds are interviewed and form stage 0 of the sampling process. The seeds identify other members of the population. The members identified in the next generation (stage 1) are approached and then asked to identify other members. This process is continued until the desired sample size is reached.

This method has been effectively utilized in a myriad of cardiac studies. For example, Gustaffson and colleagues used both convenience and snowball sampling to recruit occupational therapists working in stroke in order to investigate information provision to clients with stroke.(9) A study in 2009 used snow-ball sampling to recruit immigrant Arabic, Turkish, and Iranian women living in Australia, so as to explore the relationship between causal attributions of risk factors for CHD and physiological status.(10) Rankin and Bhopal in 2001 conducted a crosssectional study comparing the snowball sample method to more traditional sampling.(11) Their target population was South Asian residents aged 16 to 74 years living for at least a year in South Tyneside (UK).(11) The seed population were South Asian residents in South Tyneside, whose names and addresses were provided by members of a local South Asian community group.(11) Each of these seed respondent was asked to supply the names and addresses of five additional residents of South Asian descent.(11)

In our study, the initial seeds (sampling stage 0) were the Ontario members of the Canadian Heart Failure Network (CHFN) and other sites identified by the expert panel (Table 1). Established in

1999, the CHFN is a network of academic and community based clinics that provide specialized care to HF patients (www.cfna.ca). Importantly, the network did not include all HF clinics in the province, thereby necessitating further sampling.

The physician or nursing lead at each clinic was approached and a semi-structured interview conducted to establish the scope of the practise. In addition, the lead was asked to identify any other HF clinics, which may serve patients in the vicinity (1st sampling stage). We continued to accrue new sampling stages until no new clinics were identified, at which point the sample was saturated.

In 2006, the Ontario Ministry of Health and Long-Term Care transferred the responsibility for planning, integrating and funding of health services within the province to 14 regional Local Health Integration Networks (LHIN). The boundaries of each LHIN were used to assess any geographic inequalities in access to HF clinics.

Semi-structured Interviews

In order to describe the current service model at an identified HF clinic, a structured interview was conducted with the lead physician/nurse at each site. The interview ascertained information broadly on the characteristics of the clinics themselves (total number of patients, facilities, general model), and the program service model. We used a validated questionnaire developed by Reigel and colleagues to measure the intensity and complexity of each clinic's program service model across 10 categories.(12) The psychometric properties of the HF Disease

Management Scoring Instrument (HF-DMSI) has been tested, and it has content validity and an excellent interrater reliability with a intra-class correlation coefficient of 0.918.(12) The categories and the respective scoring algorithm are found in Table 2.(12) Briefly, the HF-DMSI focused on the composition of the HF team (single practitioner vs multi-disciplinary team) and the content of the HF intervention such as education (scored from 0 to 4, with 4 as the more comprehensive education program), and medication management (scored from 0 to 3). The environment of the HF clinics was categorized as those that only focused on inpatients with HF (score of 1) versus those that focused only on outpatients seen in clinic (score of 2), those that were home-based with the intervention taking place in the patients' residence (score of 3), with clinics that had components in more than 1 setting receiving the highest score of 4. Peer support, remote monitoring, and the duration and complexity of contact were also measured. The instrument was designed to provide a separate score for each category, and therefore does not provide single, overall summary score, with appropriate weights for each of the 10 categories.

Because the HF-DMSI does not provide an overall summary score, and could not be used to rank clinics, we performed a concept mapping exercise, using an HF expert panel. The concept mapping exercise consisted of two parts (13;14). In part 1, we determined the relative importance of each of the 10 categories of the HF-DMSI, based on consensus of the expert panel. In the second part, each of the clinics identified were categorized by the expert panel into three intensity groups, based on their scores on the HF-DMSI, influenced by the implicit weighting system revealed in part 1. Further description of this process is found in Appendix A.

Institutional Review Board

The ethics review board of the University of Toronto approved this protocol. When required by local institutional regulations, separate institutional review board approval was acquired for each participating clinic. Consent for the use of the structure survey results was obtained from the physician lead for each identified HF clinic.

Results

HF Clinic Identification

A total of 34 clinics were identified through our sampling method, as seen in Figure 1. From the initial 15 seed clinics identified through the CHFN, three generations of snow-ball sampling took place, at which point the sample was saturated. In addition, 5 clinics were identified through the CCN and only one additional clinic through contacting individual hospitals. Of these clinics, 30 agreed to participate in the semi-structured survey.

Regional Distribution of HF Clinics

The initial seed clinics were located in 9 of the Ontario 14 LHIN's. We were able to identify HF clinics in all the remaining LHINs except for the Central West and Erie St Clair LHINs. Access to HF clinics was not uniform across the province. As apparent from Figure 2 and Table 3, the identified HF clinics were concentrated in the south and central regions of the province. Each HF clinic served an average population of 353,800 with an over 65-year-old population of 45,200. There was a substantial range in the population served by each HF clinic, from 179,200 per clinic in the Toronto Central LHIN, to 761,400 in the central LHIN.

Clinic Characteristics

Identified HF clinics had substantial variation in their characteristics and the services offered. Identified HF clinics had substantial variation in their service volume, with a mean of 138 new consults (median 78; interquartile range 25-128) and 1020 visits per year (median 675; interquartile range 200-1479). The majority (80.6%) of clinics were physically based in hospitals with 25.8% being part of an academic institution.

In total, 143 HF clinic physicians worked at the 30 identified clinics. The clinics were run by between 1 to 8 physicians and 1 to 3 nurses. The majority of the physicians were cardiologists with 80.6% having formal training in HF management.

Access to Allied Health Professionals

The clinics had on average limited access to in-clinic allied health professionals, as seen in Table 4. Under half had such access to dieticians or pharmacists, with only 6.5% and 16.1% with in-clinic access to physiotherapists or counsellors. 87.1% of HF clinics had a formal affiliation with a cardiac rehabilitation program and 64.5% where actively involved with chronic disease management of another condition, such as diabetes mellitus.

Intensity and Complexity

The ranges of HF clinic scores on the HF-DMSI are shown on Figure 3. There was little variation between the clinics for some elements of the instrument. such as intervention duration (all scored 4; greater than 6 months) and environment. The majority of HF clinics had a formal medication management protocol, where medications were monitored and an attempt was made to increase utilization of evidence-based medications with monitoring and followup. There was substantial range in the intensity of education and counselling aimed at supporting self-care. Although all clinics had some form of education program, these ranged from programs that focused only on adherence to more comprehensive programs that emphasized surveillance, management and evaluation of symptoms in addition to treatment adherence. The majority of

clinics did not use remote monitoring at the clinic, although half did contact patients by telephone in between face-toface evaluations. A formal peer support component that was integral to the program was identified in only one HF clinic. Somewhat surprisingly, although the delivery personnel at the clinic were multidisciplinary in approximately 50% of clinics, some had only either a single generalist or HF expert provider. All of the clinics were ambulatory based, with one that was predominantly focussed on inpatients. None were exclusively home-based or had a home-based component.

Concept Mapping

Based on our concept mapping exercise, the expert panel categorized the 30 identified clinics into three strata of intensity; 8 clinics were assigned to the low intensity category, with 12 in the medium intensity category and 10 in the high intensity group. The mean scores on the HF-DMSI for these three strata are shown in Table 5. Although the 10 high intensity clinics had higher mean scores in 9 of the 10 HF-DMSI categories, this was most pronounced in the education and counselling, medication management, delivery personnel and complexity categories. This suggests an implicit weighting of the categories by our expert panel as revealed by the concept mapping exercise. This implicit weighting places a priority on a more comprehensive approach to medication management and education, HF clinics consisting of a multi-disciplinary team with multiple contacts between the team and the patient. In contrast, remote monitoring was not felt to be of particular

importance, nor was the presence of a structured peer-support program.

Discussion

In this environmental scan of HF clinics in the province of Ontario, Canada, we were successfully able to identify 34 HF clinics. However, there was substantial geographic variation in terms of access to HF clinics, with no HF clinics identified in 2 LHIN's. As anticipated, the clinics were varied in structure and the services offered. The greatest variation in terms of intensity and complexity was in terms of the education service offered. Remote monitoring and a home-base component to the HF clinic services were notably absent in most clinics.

Multi-disciplinary ambulatory complex disease management clinics are increasingly studied as the preferred modality of ambulatory care delivery for chronic diseases such as HF.(1;3;4;6) Advocates of such clinics highlight the many randomized clinic trials that show the efficacy of such clinics in reducing mortality and rehospitalizations.(3;15-20) Importantly, although these clinics are grouped together in systematic reviews and meta-analyses, there is heterogeneity in the models evaluated and services offered. Prior to implementing these clinics in routine practise, it is critical to understand which components are central to the intervention. Moreover, in evaluating the effectiveness of HF clinics currently in operation, it is important to compare the services offered currently with those studied, to determine if the results from the published literature are applicable.

Several meta-analyses have addressed this research question (3;15-20). McAlister and colleagues evaluated 29 trials enrolling a total of 5,039 patients (3). Because of substantial

heterogeneity, they did not report an overall summary statistic (3). They found that multi-disciplinary clinics improved mortality, and hospitalization, while tele-monitoring improved rehospitalization rates (3). Holland and colleagues contrasted studies that incorporated home visits, or between visits telephone calls, to those that were solely hospital or clinic based (18). In the 30 trials that were included in their analysis, they found that reductions in hospitalization were limited to studies that included either a home-based or telephone based component to the intervention.

The heterogeneity of the literature is insightful, in that it implies that one cannot equate one HF clinic model with another. Instead the specific components of the intervention are key. To this end, two notable issues arise from our environmental scan of Ontario clinics: first, remote monitoring and a patient home component is absent in most clinics. Second, the intensity of education services is highly varied. This suggests that one cannot simply apply the efficacy data from randomized controlled trials to real world HF clinics, but rather, the effectiveness of these clinics need to be established independently. This is a key area for further research.

A central tenet of the Canada Health Act is uniform accessibility to care. Our environmental scan suggests that there is substantial disparity in access to HF clinics across the province of Ontario. This may be potentially explained by regional variations in the incidence and prevalence of HF; however, the absence of specific MOTHLC funding for the HF

clinics may be an importantly contributing factor. Elucidation of the underlying mechanisms for this disparity will be important for policy makers.

Our study must be interpreted in the context of several limitations. First, although we used a number of different methods to locate all HF clinics in the province, we cannot confirm that all clinics were in fact identified. We used an instrument to evaluate intensity and complexity; this did not cover all potential service components. Indeed, it does not include post-discharge planning, which has been identified by some studies as a critical component to reduce early rehospitalisation. Finally, although we have categorized clinics into intensity strata based on expert opinion, the relevance of such categories is dependent on their association with improved patient outcomes.

In summary, through our environmental scan, we found that despite the absence of specific governmental funding, there are at least 34 HF multidisciplinary clinics in operation in the province of Ontario. These clinics have a wide range of services offered. Further research on understanding which of these service components are critical to improved patients outcomes will aid policy makers and clinicians to determining the optimal care model for these complex patients.

Table 1: Seed Heart Failure Clinics

Clinic Name and Location

1. Cornwall: Cornwall Community Hospital

- 2. Hamilton: Heart Function Clinic Hamilton Health Sciences Corporation
- 3. Kingston: Hotel Dieu Hospital
- 4. Kitchener: St. Mary's Hospital
- 5. London: London Health Sciences Centre
- 6. Oakville: Oakville-Trafalgar Memorial Hospital
- 7. Orillia: Orillia Soldiers' Memorial Hospital
- 8. Ottawa: University of Ottawa Heart Institute
- 9. Owen Sound: Grey Bruce Health Services
- 10. Picton: Prince Edward Family Health Team CHF Clinic
- 11. Toronto: University Health Network (UHN) (1)
- 12. Toronto: University Health Network (UHN) (2)
- 13. Toronto: Mt Sinai Heart Function Clinic
- 14. Toronto: St Michael's Hospital Heart Function Clinic
- 15. Toronto: Sunnybrook Hospital Heart Function Clinic

 Table 2: Heart Failure Disease Management Scoring Instrument (HF-DMSI)

Intervention category	Points to be assigned
Recipient	1=Provider alone 2=Patient alone 3=Patient with some inclusion of caregiver 4=Patient with a caregiver who is central to the intervention
Intervention content	
Education and counselling aimed at supporting self-care	0=No mention of education 1=Focus solely on importance of treatment adherence 2=Focus on treatment adherence including some creative methods of improving adherence 3=Focus on surveillance but no mention of actions to be taken in response to symptoms (eg, no flexible diuretic management) 4=Emphasis on surveillance, management, and evaluation of symptoms in addition to treatment adherence
Medication management	0=No mention of medication regimen 1=Some mention of medications (eg, importance of medication compliance) but not an active part of the intervention. No attempt to intervene with provider to get patients on an evidence- based medication regimen 2=Evidence-based medication regimen advocated but no follow-up with patient or provider to monitor the suggestion 3=Medication regimen monitored, attempt made to get the patient on evidence-based medications, with follow-up monitoring done with patient or provider
Social support Peer support	0=No mention of a peer support intervention 1=Peer support mentioned but not integral to intervention 2=Peer support integral component of intervention
Surveillance by provider: Remote monitoring	0=No use of remote monitoring or telehealth 1=Remote monitoring is used in conjunction with other interventions that form the main intervention used 2=Telehealth is essential component of intervention
Delivery personnel	1=Single generalist provider (eg, physician, nurse, pharmacist) 2=Single HF expert provider (eg, physician, nurse, pharmacist) 3=Multidisciplinary intervention
Method of communication	1=Mechanized via internet or telephone 2=Person-to-person by telephone 3=Face-to-face, individual, or in a group 4=Combined: Face-to-face at least once alone or in a group with individual telephone calls in between meetings
Intensity and complexity	
Duration	$1 = \le 1 \text{ mo}$ $2 = \le 3 \text{ mo}$ $3 = \le 6 \text{ mo}$ 4 = > 6 mo
Complexity	1=Low: single contact with little or no follow-up 2=Moderate: >1 but <4 and/or infrequent contact or contacts of short duration 3=High: multiple contacts of significant duration
Environment	1=Hospital: Inpatient only 2=Clinic/outpatient setting 3=Home-based 4=Combination of settings

Table 3: Geographic Distribution of Clinics

LHIN	# HF Clinics	Total Populaton	population per HF Clinic	age 65yrs and over per LHIN	>65 population per HF clinic
Erie St. Clair	0	623,300	NA	85,000	NA
South West	3	890,100	296,700	125,800	41,900
HNHB	2	1,298,300	649,100	192,400	96,200
Waterloo Wellington	5	679,700	135,900	76,000	15,200
Mississauga Halton	3	1,002,300	334,100	103,400	34,500
Central West	0	735,200	NA	65,900	NA
Central	2	1,522,800	761,400	183,100	91,600
Central East	3	1,419,800	473,300	184,600	61,500
Toronto Central	6	1,075,100	179,200	131,800	22,000
North Simcoe Muskoka	3	417,000	139,000	59,900	19,967
South East	2	457,200	228,600	74,700	37,350
Champlain	3	1,131,400	377,100	137,600	45,900
North East	1	545,000	545,000	84,900	84,900
North West	1	231,900	231,900	31,400	31,400
Total	34	12,028,900	353,800	1,536,500	45,200

LHIN: Local Health Integration Network; HF: Heart Failure; HNHB: Hamilton Niagara Haldimand Brant

Table 4: Characteristics of 30 identified clinics

Parameter	
PERSONEL	
Mean number of Physicians	4.7 (1-8)*
% cardiologist	80.6
% internists	22.6
% family physicians	9.7
% Heart failure training	80.6
Mean Number of Nurses	2.0 (1-6)*
LOCATION	
% Academic	25.8
% Community Based	74.2
Mean Annual Total Visits	1020 (200-1479)*
Mean Annual Total New Patients	139 (25-128)*
% Access to Onsite Echocardiography	80.6
% Access to Onsite Nuclear Cardiology Testing	58.1
% Access to Onsite Angiography	38.7
% Access to Onsite Exercise Stress Testing	77.4
Mean Exam Rooms	3.3 (1-4)*
ALLIED HEALTH PROFESSIONALS	
% Access to Dietician (In Clinic)	45.2
% Access to Pharmacist (In Clinic)	32.3
% Access to Physiotherapy (In Clinic)	6.5
% Access to Counselor (In Clinic)	16.1
% Affiliated with Cardiac Rehabilitation	87.1
% Involved in other Disease Management	64.5

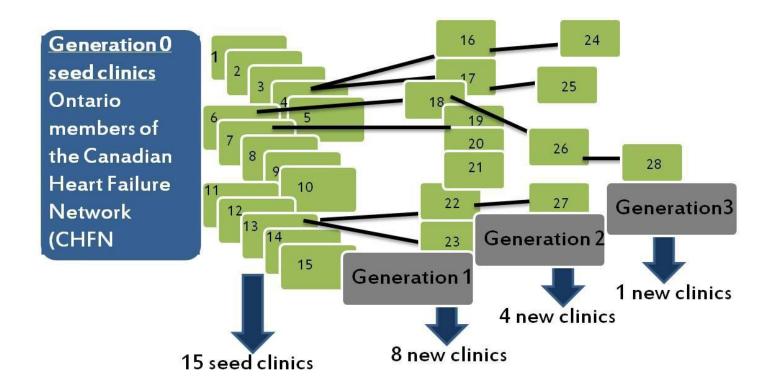
^{*}inter-quartile range is shown

Table 5: Clinic Intensity and Complexity

	All clinics	Clinic intensity types			
HF-DMSI category	(n = 30)	High	Medium	Low	
	$(\Pi = 30)$	(n = 10)	(n = 13)	(n = 7)	p-value
Recipient	3.3±0.6	3.7±0.5	3.2±0.6	3.0±0.6	.040
Education and counselling	3.2±1.0	3.9±0.3	3.1±1.0	2.6±1.1	.011
aimed at supporting self-care					
Medication management	2.7±0.5	3.0±0	2.8±0.4	2.1±0.7	.002
Peer support	0.3±0.5	0.6±0.7	0.2±0.4	0.3±0.5	.147
Remote monitoring	0.7 ± 0.8	1.0±0.8	0.8 ± 0.8	0.1±0.4	.079
Delivery personnel	2.5±0.6	3.0±0	2.5±0.5	2.0±0.8	.002
Method of communication	3.6±0.5	4.0±0	3.5±0.5	3.4±0.5	.018
Duration	4.0±0	4.0±0	4.0±0	4.0±0	-
Complexity	2.6±0.6	3.0±0	2.6±0.5	2.0±0.6	<.001
Environment	2.0±0.2	2.0±0	1.9±0.3	2.0±0	.536

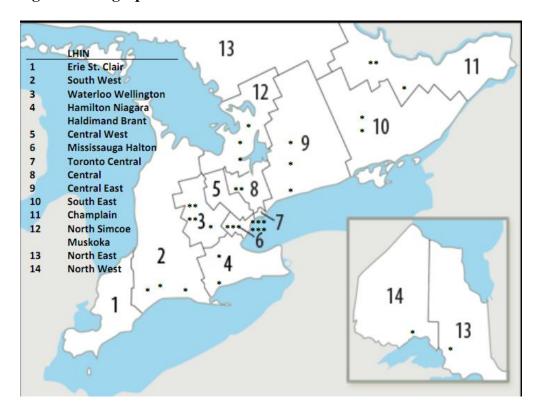
HF-DMSI: Heart Failure Disease Management Scoring Instrument * Results are presented as means \pm standard deviations. Please refer to Table 2 for detail description of HF-DMSI categories and scoring.





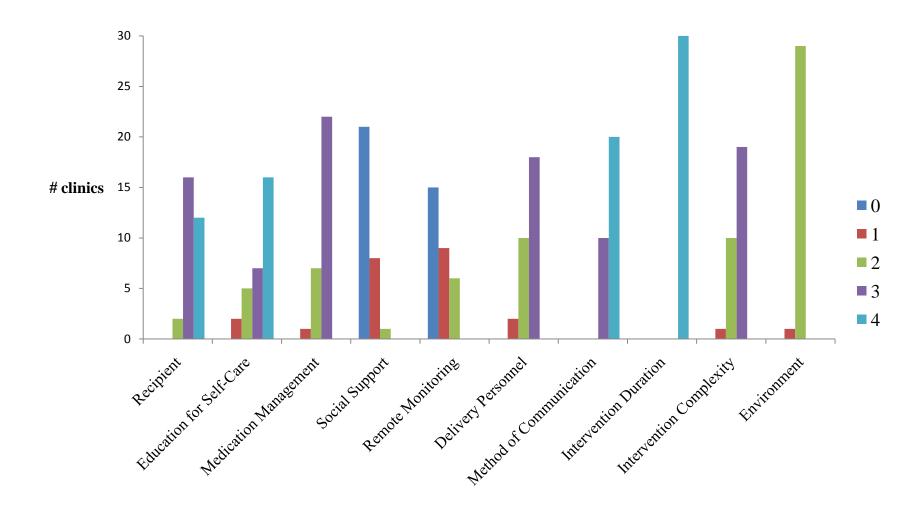
Saturation was reached in 3 generations. In total, 28 clinics were identified via snowball sampling. A total of 5 Heart Failure (HF) clinics were identified via the Cardiac Care Network (CCN) and 1 HF clinic via systematic calls for a total of 34 HF clinics.

Figure 2: Geographic Distribution of Heart Failure Clinics



Regional Local Health Integration Networks (LHIN) in Ontario depicting initial 15 seed clinics and hidden clinics identified via sampling.

Figure 3: Scores on Heart Failure Disease Management Scoring Instrument (HF-DMSI)



Appendix A

Heart Failure Clinic Stratification using Concept Mapping

Once the surveying of all the clinics was completed, this categorization process was revealed to be complex and nuanced. The initial conceptualization was that the clinics would be categorized by complexity and intensity of intervention. While the HF-DMSI developed by Riegel and colleagues is useful in capturing the richness of the multi-attribute, multi-domain activities of a heart failure clinic, it is not an instrument which provides a summary score that could be used to rank the clinics.(12) To overcome this limitation, a concept mapping exercise was conducted consisting of two parts.

The first part was a priming exercise where the relative importance of the measured elements of the HF-DMSI was determined by a multidisciplinary expert panel. The second part was a categorization of the scored clinics into three intensity levels based on their scores on the HF-DMSI instrument and the implicit weighting of the HF-DMSI elements in the first part of the exercise.

This technique was pioneered by psychologist George Kelly whereby the categorization of many elements could be reliably and stably obtained through and exercise called a "card sort".(13) This technique has been found to be reliable and robust and is used frequently in software design, taxonomy development and other fields where multi-attribute categorization or stratification is required.(14)

There are two types of card sort – open and closed. An open card sort requires that the individual or group create

categories themselves from the elements to be sorted – the number of categories is open, as is any labelling of those categories. A closed card sort provided a pre-specified set of categories to which all elements must be assigned.

For the categorization of the heart failure clinics we used a closed card sort in two parts. We gathered a multi-disciplinary panel of experts working in heart disease management and treatment, as well as a several people working in heart failure clinics in different capacities. This provided us with a panel with broad knowledge of the subject area, rich experience and deep, relevant professional knowledge of cardiac care in general and heart failure clinics specifically.

In the first part of the closed card sort we needed to prime the process based on the elements described in the HF-DMSI. For this purpose we decomposed each of the ten elements of the instrument into their descriptive components. For instance, in the element of "Social Support/Peer Support" there are three components; "No mention of a peer support intervention", "Peer support mentioned but not integral to intervention" and "Peer support integral component of intervention". These components, stripped of their scoring values, where then placed by group consensus into the three categories – high, medium and low. Although this process may seem trivial, it often led to splits that were not obvious before the discussion. Especially in the division of four- and five-component elements we found that the development of a consensus was instructive. At the end of the priming exercise we had placed all

38 descriptive components into one of the three categories. This stratification provided the framework for the second part of the card sort.

In the second part of the card sort we utilized the concepts mapped in the first part to inform the categorization of each clinic into High, Medium and Low service categories. To do this we took each clinic, identified only by a random number, and created based on scores on the HF-DMSI, a narrative description of that clinic, using the descriptive components that were actually ascribed to those clinics in the survey process. This meant that the same set of descriptive attributes categorized in the first part of the exercise were used as markers of clinic activity for the purposes of categorization. For simplicity, the capsule descriptions only included eight of the 10 elements from the HF-DMSI, as all 30 clinics shared the same scores on two elements. We then assigned each clinic to one of the High, Medium or Low service strata through a consensus-generating process. Chapter 3: Insights into the Contemporary Management of Heart Failure in Specialized Multi-Disciplinary Ambulatory Clinic

Objective

The objective of Phase 3 was to understand the practise patterns and process of care within the identified clinics. Specifically, we were interested in variations between HF clinics in the prescription and optimal dosing of evidence based medications.

Methods

Clinic Selection

The study was part of a larger comprehensive field evaluation that assessed the scope and efficiency of services offered by existing HF clinics in Ontario. The first phase of the project identified 34 existing HF clinics in Ontario. These HF clinics were subsequently classified as high, medium or low intensity, based on scores on the HF Disease Management Scoring Instrument (HF-DMSI), a validated instrument to evaluate the intensity and complexity of services at HF clinics (12). In this study, three clinics were randomly selected from each intensity strata (high, medium and low).

Chart Abstraction

Chart abstraction was conducted by experienced nurses, using computerbased chart abstraction forms. We randomly selected 100 patient medical records from each clinic. Information abstracted from the medical records included patient baseline demographic and clinical data, as well as medical diagnostic testing, and specialist referrals. Of particular interest was information on medication classes and doses on first visit, and any subsequent medication changes. Charts were reviewed for up to 1 year from the first clinic visit, or until death, which ever event occurred first.

Each abstractor was provided with a study laptop computer supporting only the applications required for the study, and equipped with encryption software for data collection. This high-level of security ensured protection of patient confidentiality. Data was entered into an offline chart abstraction interaction software supported by THETA.

Nurse abstractor candidates underwent extensive training, including a detailed session on definitions of data variables, supported by practice abstraction on sample charts, and feedback on their chart abstraction skills. Abstractors were hired for the project only if they demonstrated a high standard for accuracy and completeness. A study manual with written definitions for each variable of interest and guidelines was provided to all participants to support standardized data collection.

Analytic Plan and Study Definitions

i. Description of Patient Populations
The first part of this study was
descriptive in nature. We compared the
demographic and clinical characteristics
of the patients seen at the 9 HF clinics.
In addition, we contrasted the number of
clinic visits, diagnostic test performed
and overall medications prescribed.
Because the charts abstracted included
patients first seen anytime between 1995
and 2010, we compared patients who
were seen initially between 1995 and
2005 (early cohort) vs. those seen after
2005 (recent/contemporary cohort) to
understand temporal changes in practise.

ii. ACEi/ARB & β-Blocker Use
Our primary analyses evaluated the uptake of β-blockers, and angiotensin converting enzyme inhibitors (ACEi) and/or angiotension receptor blockers (ARB). We focused on these medications given the strong evidence base for their use in HF (1). As a secondary endpoint, we assessed the proportion of patients on either β-blockers, or ACE-inhibitors/ARB who were taking specific medications within the class that were recommended by practise guidelines and if these

medications were titrated to optimal doses (1). The list of recommended medications and their corresponding target doses is found in Appendix A.

Statistical Analyses

Statistical analyses were conducted using SAS version 9.2 (SAS Institute Inc, Cary, North Carolina). Continuous data was compared between HF clinics using the ANOVA test and categorical data using the chi-square or Fisher's exact tests.

Patient and clinic level predictors to medication prescription (β -blockers or ACEi/ARB) and ever achieving the target dose during the follow-up period were assessed using hierarchical logistic regression model. Multi-level modelling was required, as we anticipated that patients seen at the same clinic may be similar; hierarchical models take account of such clustering. All p-values less than 0.05 were considered statistically significant.

Institutional Review Board

The ethics review board of the University of Toronto approved this protocol. Separate institutional review board approval was obtained for each participating clinic.

Results

Baseline Characteristics of HF patients

A total of 902 patients were randomly selected from 9 clinics, with approximately 100 charts abstracted per clinic. Baseline characteristics of these patients are found in Table 1. As is apparent from this table, there was substantial heterogeneity in the clinical characteristics of the patients seen across clinics, most notably in mean age, symptom severity, HF etiology and comorbidities.

The mean age of identified patients was 66.1 years, with a statistically significant range of means between clinics from 53.5 years to 75.1 years. The majority of patients were males (64.5%). Mean left ventricular ejection fraction (LVEF) was 32.9% and the majority of patients were moderately symptomatic with New York Heart Association (NYHA) functional class of II (30.6%) or III (27.5%). However, symptom severity was only reported in 72.2% (n =651) of patients. Similarly, the underlying etiology for HF was inconsistently reported, with only 477 patients (52.9%) having this reported. Of these, 58.5% had an ischemic cardiomyopathy, again with substantial range between clinics.

Approximately half of patients had documented hypertension (61.7%) and hyperlipidemia (56.9%). As seen in Table 1, there was a statistically significant difference between the 9 clinics as far as the proportion with these co-morbidities. In contrast, 37.4% of patients had diabetes mellitus, with less range between clinics.

There was a substantial difference in the clinics in terms of the proportion of

patients with atrial fibrillation (AF). In four clinics, none of the patients abstracted had AF, while in others, almost 20% did. On average, the proportion of patients with AF among the 902 abstracted charts was 9%.

Clinic Visits and Diagnostic Tests

Over the 1 year time-horizon of the chart abstraction, patients had an average of 4.3 clinic visits. However, there was substantial variation, with patients abstracted from Clinic #5 having only 2.8 visits on average, while those in Clinic #1 having 6.7 visits (see Table 2).

There were statistically significant differences in terms of diagnostic tests performed. Overall, 77.3% of patients had an echocardiogram during the study period. However, this ranged from 42% to 95% between clinics. Similarly, angiography ranged from 19% to 62% (mean of 38.4%). Natriuretic peptides were used infrequently in the majority of clinics, with only 7% of all patients having documentation of use. In Clinic #9 however, 21% of patients had natriuretic peptides measured.

Medication Use

Summary of medication prescriptions are shown for the overall group and per clinic in Table 3. The majority of patients were receiving ACEi/ARB therapy at 88.2%, with little difference between the clinics. Although, β -blocker use was excellent, at 85.3% for the overall group, there was a statistically significant difference between clinics, with a range from 76% to 89%. Similarly, aldosterone antagonists were used in 35.4% in the overall group, with significant range from 26% to 53%.

There were substantial differences among clinics in the use of other HF and cardiac medications, as seen in Table 3. The majority of patients were on loop diuretics, with 29.9% on digoxin. Approximately half were on statins, with 54% on anti-platelet agents, roughly approximating the proportion of patients with an ischemic etiology for their cardiomyopathy.

Comparison of Early vs. Recent Cohorts

Of the 902 patients, 579 were in the recent cohort, with a first clinic visit after 2005 (Table 7). Figure 1 shows the proportion of patients per clinic that were either in the early or recent cohort. In comparison to patients seen in the earlier era, more recent patients tended to be older, with a higher mean LVEF (33.6 vs 30.9%; p-value 0.0187). In addition, more recent patients had a higher proportion of patients with renal dysfunction, hyperlipidemia and hypertension (table 7).

A higher proportion of the recent cohort patients underwent coronary angiography, with no difference in the proportion with echocardiograms or natriuretic peptide use (Table 8).

Somewhat surprising, ACE/ARB use was lower in the recent cohort (85.8%) compared to the early cohort (95.6%) with no difference in β -blocker use. Digoxin was also less common in the recent cohort (26.8% vs 35.6%; p-value 0.0055) (Table 8).

Target Doses of ACEi/ARB and β-blockers

We sought to understand if there were differences in the type and dosage of

ACEi/ARB and β -blockers. As seen in Table 4, there were important differences. 52.8% of patients were on target doses of recommended ACEi/ARB (see appendix A). This ranged from 43.0% to 90.0% among the clinics.

β-blocker use was more varied, with only 27% of patients on target dose, with a range from 16% to 51% between the nine clinics.

Predictors of ACEi/ARB and β-blocker use

In Table 5, we explored patient and clinic level characteristics associated with being prescribed an ACEi/ARB or β -blocker. In the univariate analyses, as expected, we found that lower LVEF was significantly associated with an increased probability of being on either medication class.

Patients with renal dysfunction were less likely to be on ACEi/ARB with an odds ratio (OR) of 0.351 (95% confidence interval (CI) 0.221-0.558; p-value <0.001).

In the multi-variable model, having adjusted for patient level differences, we found that clinics with physicians who had HF training were more likely to prescribe β-blockers and ACEi/ARB.

However, when evaluating the likelihood of being on target doses of either medication class, we were not able to identify any clinic level characteristic that was a statistically significant predictor. The only consistent patient level predictor was age, where increasing age was associated with a lower probability of being on target doses of these medications. For ACEi/ARB, having hypertension and

diabetes was associated with an increased likelihood of being on target dose, with an OR of 1.477 and 1.465 respectively.

Discussion

In this chart abstraction of 902 HF patients, we sought to understand if there were important differences in the patients seen across a subset of HF clinics across the province, and evaluate the degree of heterogeneity of the patients' journey through this ambulatory care intervention. We found substantial variation in the characteristics of patients seen at clinics, the diagnostic tests performed, and the medications administered. This work is complementary to our earlier work suggesting that the service models for clinics across the province of Ontario have substantial variation in terms of complexity and intensity.

The patients are HF clinics abstracted in this study were substantial younger with more males than that of the typical HF patient in Ontario. The mean age in our cohort was 66 years, with almost 2/3s being male. In contrast, the mean age of HF patients discharge alive in Ontario is approximately 77 years, with 48% being males. This likely is reflective of the referral biases of providers, and is consistent with the treatment-risk paradox seen in other areas of medicine, where older patients with greater comorbidities, despite the potential benefits of an efficacious intervention. do not receive it (21).

The differences in the number of clinic visits over the period of abstraction were marked, with a 2.5 fold difference. This may reflect differences in the scope of practise of the HF clinic. Our previous work suggests that although the majority of HF clinics in Ontario essentially took over HF-related care, some clinics function principally to provide advice to the primary care physician or general

cardiologists. One would expect fewer visits in HF clinics with the latter scope of practise.

Similarly the differences in diagnostic testing may reflect ease of access. For example, although 80% of clinics were physically located within a hospital, only a minority had access to on-site cardiac catheterization facilities.

Our chart abstraction was over a 1 year time horizon after the first clinic visit. As such, this afforded a unique opportunity to evaluate temporal changes in clinical practise. We found that more recent HF clinic patients tended to be older with a higher LVEF. This in turn may explain the finding that a lower proportion of patient in the recent era (after 2005) were on ACEi/ARB given that this medications are principally of benefit in patients with reduced LV systolic function.

Potential mechanisms by which the benefits of a multi-disciplinary strategy in HF is mediated includes improved utilization and compliance with evidence-based medications.(3) In our analysis, we found reassuringly high uptake in the use of ACEi/ARB and β -blockers, the two key foundations of pharmacologic therapy in this condition.

Our secondary hypothesis was that HF clinics not only improve the uptake of evidence-based medications, but also ensure optimal dosage, such that the full benefits of these medications could be realized. We found substantially more variation among clinics, with some clinics showing a preference for strictly defined evidence based medications,

while others appeared to favour a class effect for ACEi/ARB and β -blockers. However, we were not able to identify any clinic-level predictors of this difference in practise.

Several limitations of our study merit discussion. First, despite the use of highly trained abstractors and a tested abstraction sheet, there were a relatively high proportion of missing values. This was especially concerning for variables such as NYHA class and LVEF, key prognostic indicators in HF. Second, due to budget and time constraints, we limited our abstraction to information in a 1 year time horizon. As such, we may be underestimating the final proportion of patients on target doses of medication, if titration took place over a long period. Finally, although our overall cohort was large at 902 patients, when evaluating clinic level characteristics, a key objective, our sample size was only the 9 clinics. This may have impacted our statistical power to show any differences between clinics.

In conclusion, we found that patients treated at a sub-set of the specialized HF clinics in Ontario have important differences in terms of who is seen at the clinic, and the care provided. An important area for further research is elucidation of how these differences may impact health outcomes.

Table 1: Baseline Characteristics

Characteristics*	All N =902	(n = 100)	(n = 100)	3 (n =99)	4 (n =102)	5 (n = 100)	6 (n = 100)	7 (n = 101)	8 (n = 100)	9 (n = 100)	P- value
Age (years), mean ± sd (range 17-95)	66.1±15.7	75.1±10.8	71.5±11.6	65.4±16.5	69.7±12.0	61.5±14.2	71.4±14.0	56.2±19.0	69.7±14.0	53.5±13.8	<.0001
Male	570 (64.5)	59(59.0)	63(63.0)	73(73.7)	66(66.0)	68(68.7)	62(62.0)	56(63.6)	64(64.0)	59(60.2)	.5296
HF mode Ischemic Non-ischemic	279 (58.5) 198 (41.5)	6 (42.9) 8(57.1)	37 (75.5) 12 (24.5)	48 (59.3) 33 (40.7)	52 (62.6) 31 (37.4)	23 (74.2) 8(25.8)	23 (63.9) 13 (36.1)	30 (50.9) 29 (49.1)	25 (55.6) 20 (44.4)	35 (44.3) 44 (55.7)	.0121
NYHA class I II III IV	92 (14.1) 276 (42.4) 248 (38.1) 35 (5.4)	2(2.2) 39(43.3) 46 (51.1) 3 (3.3)	10(12.1) 38 (45.8) 29 (34.9) 6 (7.2)	14(16.3) 45(52.3) 25(29.1) 2 (2.3)	19(20.2) 36(38.3) 36(38.3) 3 (3.2)	12(12.3) 48(49.5) 34(35.1) 3(3.1)	0 6(46.2) 6(46.2) 1 (7.6)	12 (13.2) 27 (29.7) 41 (45.1) 11(12.1)	3 (21.4) 5(35.7) 3 (21.4) 3(21.4)	20(24.1) 32(38.6) 28(33.7) 3(3.6)	.0002
LVEF (%), mean ±sd	32.9±14.0	32.5±14.4	33.4±16.0	30.6±12.3	32.7±13.5	33.8±15.5	32.3±12.0	32.9±13.4	36.3±13.0	32.0±14.5	.4690
Hypertension	502 (61.7)	67(74.4)	43(46.7)	51(56.7)	69(74.2)	41(42.7)	80(81.6)	46(55.4)	53(61.6)	52(62.5)	<.0001
Diabetes Hyperlipidemia	300 (37.4) 452 (56.9)	34(40.5) 64(75.2)	36(38.7) 48(52.2)	34(37.4) 43(50.6)	37(40.2) 59(64.8)	37(38.5) 66(68.8)	40(40.8) 59(60.2)	22(26.5) 36(44.4)	30(34.1) 34(40.0)	30(38.5) 43(53.4)	.6562 <.0001
Renal dysfunction	137 (17.9)	14(21.2)	10(10.9)	24(27.6)	19(21.6)	5(5.2)	14(14.3)	17(20.2)	14(16.9)	20(27.8)	.0009
Liver dysfunction	17 (2.3)	2(3.3)	0	4(5.1)	3(3.5)	0	4 (1.0)	0	1(1.4)	6(9.1)	.0024
Atrial fibrillation	81 (9.0)	19 (19.0)	20 (20.0)	0	0	19 (19)	0	12 (11.9)	11 (11.0)	0	<.0001

^{*}Results are presented as frequencies and percentages unless specified otherwise. Percentages were calculated after excluding the missing values. HF: heart failure; NYHA: New York Class Association; LVEF: left ventricular ejection fraction

 Table 2: Diagnostic Test Performed over 1 year of chart abstraction

Characteristics*	All N =902	1 (n = 100)	2 (n = 100)	3 (n =99)	4 (n =102)	5 (n = 100)	6 (n =	7 (n =	8 (n = 100)	9 (n = 100)	P-value
							100)	101)			
Echocardiogram	697(77.3)	42(42.0)	77(77.0)	85(85.9)	88(86.3)	80(80.0)	69(69.0)	95(94.1)	72(72.0)	89(89.0)	.<0001
Coronary Angiogram	346(38.4)	26(46.0)	34(34.0)	49(49.5)	51(50.0)	31(31.0)	19(19.0)	51(50.5)	23(23.0)	62(62.0)	.<0001
Natriuretic peptide	62(7.0)	10(10.0)	0	2(2.0)	3(2.9)	4(4.0)	5(5.0)	17(16.8)	0	21(21.0)	<.001
Clinic visits	4.3 ± 3.9	6.7 ± 5.9	3.7 ± 2.5	4.8 ± 3.5	4.9 ± 4.9	2.8 ± 1.6	3.5 ± 2.1	3.1 ± 1.8	3.0 ± 2.1	3.4 ± 2.6	<.0001

^{*}Results are presented as frequencies and percentages unless specified otherwise.

Table 3: Medication ever prescribed

Characteristics	All	1	2	3	4	5	6	7	8	9	P-value
	N = 902	(n = 100)	(n = 100)	(n = 99)	(n = 102)	(n =	(n =	(n =	(n = 100)	(n = 100)	
						100)	100)	101)			
ACEi	753(83.5)	78(78.0)	89 (89.0)	83(83.8)	84(82.4)	88(88.0)	80(80.0)	86(85.2)	83 (83.0)	82 (82.0)	0.5121
ARB	68(7.5)	5(5.0)	3 (3.0)	10(10.1)	15(14.7)	9(9.0)	5(5.0)	7(6.9)	4 (4.0)	10 (10.0)	0.0386
ACEi/ARB	796(88.2)	82(82.0)	90 (90.0)	89(90.0)	92(90.2)	95(95.0)	84(84.0)	90(89.1)	86 (86.0)	88 (88.0)	.180
B-blockers	769(85.3)	81(81.0)	89 (89.0)	88(89.0)	95(93.1)	86(86.0)	85(85.0)	87(86.1)	76 (76.0)	82 (82.0)	.037
Aldosterone antagonists	319(35.4)	33(33.0)	26 (26.0)	53(53.5)	49(48.0)	26(26.0)	31(31.0)	39(38.6)	28 (28.0)	34 (34.0)	<.0001
Antiplatelets	487(54.0)	62(62.0)	68 (68.0)	42(42.4)	56(55.0)	64(64.0)	44(44.0)	55(54.5)	46 (46.0)	50 (50.0)	0.0007
Anti thrombin	356(39.5)	53(53.0)	34 (34.0)	38(38.4)	45(44.1)	40(40.0)	46(46.0)	29(28.7)	35 (35.0)	36 (36.0)	0.0219
Digoxin	270(29.9)	28(28.0)	31 (31.0)	43(43.4)	33(32.4)	21(21.0)	35(35.0)	30(29.7)	21 (21.0)	28 (28.0)	0.0202
Loop diuretics	743(82.4)	97(97.0)	93 (93.0)	92(93.0)	94(92.2)	78(78.0)	85(85.0)	70(69.3)	73 (73.0)	61 (61.0)	<.0001
Hydralazine	34(3.8)	1(1.0)	0	13(13.1)	7(6.9)	0	5(5.0)	1(1.0)	0	7 (7.0)	<.0001
Nitrates	179(19.8)	14(14.0)	22 (22.0)	31(31.3)	20(19.6)	17(17.0)	26(26.0)	8(7.92)	21 (21.0)	20 (20.0)	.0039
Statins	461(51.1)	63(63.0)	52 (52.0)	46(46.5)	65(63.7)	56(56.0)	48(48.0)	45(44.6)	41 (41.0)	45 (45.0)	0.0055

ACEi: angiotensin converting enzyme inhibitor; ARB; angiotensin receptor blocker

Table 4: Medication- Any time during the visits at target dose of evidence-based medication (among users)

Patients on evidence- based medication	All on target dose	1	2	3	4	5	6	7	8	9	P- value
ACEi/ARB (N = 762)	402 (52.8)	35(48.6)	48(57.1)	51(59.3)	39(42.9)	46(50.0)	35(44.9)	57(90.0)	42(84.0)	49(57.7)	.095
β -Blocker (N = 718)	194 (27.0)	12(16.0)	42(51.2)	38(45.8)	15(17.1)	27(32.1)	14(17.3)	16(20.5)	11(15.7)	19(24.7)	<.001

ACEi: angiotensin converting enzyme inhibitor; ARB; angiotensin receptor blocker

Table 5: Predictors of medication prescription

Covariates	Ever prescribed β -blocker OR (95% CI) (n = 902)	p-value	Ever prescribed ACEi/ARB OR (95% CI) (n = 902)	p-value
Patient characteristics at baseline visit	(single logistic regression)			
Age	1.000 (0.989 - 1.012)	0.9353	0.977 (0.963 - 0.991)	0.0019
Male	1.236 (0.822 - 1.857)	0.3084	0.940 (0.612 - 1.444)	0.7783
LVEF%	0.951 (0.936 - 0.966)	<.001	0.956 (0.940 - 0.973)	<.0001
Hypertension	1.427 (0.987 - 2.063)	0.0590	1.472 (0.980 - 2.209)	0.0623
Diabetes	1.238 (0.828 - 1.851)	0.2974	1.370 (0.873 - 2.152)	0.1713
Hyperlipidemia	1.818 (1.246 - 2.654)	0.0020	1.245 (0.829 - 1.871)	0.2906
Renal dysfunction	1.618 (0.900 - 2.909)	0.1076	0.351 (0.221 - 0.558)	<.0001
Liver dysfunction	n/a***	0.9843	0.615 (0.174 - 2.175)	0.4504
Atrial Fibrillation	2.186 (0.931 - 5.136)	0.0726	0.794 (0.405 - 1.555)	0.5006
Clinic characteristics*				
Remote monitoring (any type)	1.315 (0.621 - 2.784)	0.4168	1.472(0.778 - 2.787)	0.1950
HF training	1.845 (1.047 - 3.253)	0.0378	1.732 (1.003 - 2.992)	0.0491
Use of guidelines	0.764 (0.359 - 1.624)	0.4266	0.856 (0.439 - 1.669)	0.5991
#of nurses in the clinic	0.181 (0.065 -0.773)	0.1363	0.522 (0.112 - 3.444)	0.6013
#of physicians in the clinic	1.310 (0.088 - 19.415)	0.6983	1.558 (0.195 - 12.449)	0.6130
Academic (vs community)	0.893 (0.385 - 2.071)	0.7589	1.035 (0.473 - 2.266)	0.9208
Access to in-clinic pharmacist	1.154 (0.464 - 2.868)	0.7212	1.039 (0.465 - 2.324)	0.9138

ACEi: angiotensin converting enzyme inhibitor; ARB; angiotensin receptor blocker; LVEF: left ventricular ejection fraction; HF: heart failure *Hierarchical logistic regression model adjusted for all variables but LVEF% & liver dysfunction for BB; LVEF% for ACEI/ARB) LVEF% was excluded from hierarchical models because of missing values (168 missing out of 902). All 9 clinics had cardiologists working in the clinic and had access to on-site Echo ***Complete separation - All patients with liver dysfunction were prescribed beta blockers.

Table 6: Predictors of ever achieving the target dose of medication

Covariates	Ever on Target dose for β -blocker OR (95% CI) $(n = 718)$	p-value	Ever on target dose for ACEi/ARB OR (95% CI) (n = 762)	p-value
Patient characteristics at baseline v	risit (<i>single logistic regressi</i>	on)		
Age	0.983 (0.973 - 0.994)	0.0018	0.990 (0.981 - 1.000)	0.0434
Male	1.170 (0.816 - 1.678)	0.3929	1.214 (0.898 - 1.640)	0.2073
LVEF%	0.988 (0.972 - 1.003)	0.1153	0.997 (0.986 - 1.009)	0.6681
Hypertension	0.899 (0.646 - 1.253)	0.5306	1.477 (1.108 - 1.970)	0.0079
Diabetes	1.330 (0.945 - 1.870)	0.1018	1.465 (1.080 - 1.987)	0.0140
Hyperlipidemia	0.741 (0.533 - 1.031)	0.0751	1.108 (0.834 - 1.473)	0.4780
Renal dysfunction	1.025 (0.653 - 1.609)	0.9137	1.033 (0.679 - 1.572)	0.8782
Liver dysfunction	1.129 (0.392 - 3.247)	0.8222	0.491 (0.163 - 1.479)	0.2063
AF	1.029 (0.590 - 1.795)	0.9186	1.049 (0.630 - 1.747)	0.8541
Clinic characteristics*				
Remote monitoring (any type)	1.514 0.479 - 4.785	0.4223	0.863 (0.529 - 1.409)	0.5010
HF training	2.098 (0.695 - 6.327)	0.1566	1.350 (0.842 - 2.163)	0.1762
Use of guidelines	1.075 (0.324 - 3.561)	0.8912	0.890 (0.546 - 1.452)	0.5918
#of nurses in the clinic	1.023 (0.652 - 1.606)	0.9094	0.932 (0.784 - 1.106)	0.3624
#of physicians in the clinic	0.866 (0.682 - 1.100)	0.1976	0.949 (0.855 - 1.052)	0.2701
Academic (vs community)	0.818 (0.232 - 2.888)	0.7181	1.201 (0.707 - 2.041)	0.4413
Access to in-clinic pharmacist	0.685 (0.171 - 2.746)	0.5400	0.867 (0.487 - 1.542)	0.5755

ACEi: angiotensin converting enzyme inhibitor; ARB; angiotensin receptor blocker; LVEF: left ventricular ejection fraction; HF: heart failure; OR: odds ratio; CI: confidence interval

^{*}Hierarchical logistic regression model adjusted for all variables but LVEF%. LVEF% was excluded because missing (124 missing out of 718). All 9 clinics had cardiologists working in the clinic and had access to on-site Echo

Table 7: Comparison of patient characteristics between 1995-2005(early) and 2006-2010 cohorts (recent)

Characteristics	All N =902	Early cohort N = 323	Recent cohort $N = 579$	P-value
Age (range 17-95)	66.1±15.7	64.6±16.0	67.4±15.3	0.0005
Male	570 (64.5)	202 (63.5)	368 (65.0)	0.6556
HF mode				
Ischemic	279 (58.5)	110 (59.8)	169(57.7)	0.6499
Non-ischemic	198 (41.5)	74 (40.2)	124(42.3)	
NYHA class				
I	92 (14.1)	29 (14.5)	63 (14.0)	0.0437
II	276 (42.4)	77 (38.5)	199 (44.1)	
III	248 (38.1)	76(38.0)	172 (38.1)	
IV	35 (5.4)	18 (9.0)	17 (3.8)	
LVEF (%)	32.9 ± 14.0	30.9 ± 12.7	33.6 ± 14.5	0.0187
Hypertension	502 (61.7)	161 (57.1)	341 (64.1)	0.0504
Diabetes	300 (37.4)	97 (34.3)	203 (39.0)	0.2017
Hyperlipidemia	452 (56.9)	137 (49.3)	315 (60.9)	0.0016
Renal dysfunction	137 (17.9)	33 (12.2)	104 (21.0)	0.0025
Liver dysfunction	17 (2.3)	3 (1.2)	14 (3.0)	0.1223
Atrial fibrillation	81 (9.0)	24 (7.4)	54 (9.3)	0.3314

^{*}Results are presented as frequencies and percentages unless specified otherwise. Percentages were calculated after excluding the missing values.

HF: heart failure; NYHA: New York Class Association; LVEF: left ventricular ejection fraction

Table 8: Comparison of HF management patterns between 1995-2005 and 2006-2010 cohorts

Characteristics	All N =902	Early cohort $N = 323$	Recent cohort $N = 579$	P-value					
Procedures and tests ever done during	the visits								
Echocardiogram	697(77.3)	259 (80.2)	438 (75.6)	0.1469					
Coronary Angiogram	346 (38.4)	111 (34.4)	235 (40.6)	0.0530					
Clinic Visits	4.3 ± 3.9	3.7 ± 2.5	4.6 ± 4.4	<.0001					
Natriuretic peptide	62 (7.0)	26 (8.1)	36 (6.2)	0.2971					
Medications ever prescribed during the visits									
ACEi	753 (83.5)	287 (88.9)	466 (80.5)	0.0012					
ARB	68 (7.5)	21 (6.5)	47 (8.1)	0.3782					
ACEi/ARB	796 (88.2)	299 (95.6)	487 (85.8)	0.0026					
Aldosterone antagonists	319 (35.4)	108 (33.4)	211 (36.4)	0.3654					
Antiplatelets	487 (54.0)	157 (48.6)	330 (57.0)	0.0154					
Anti thrombin	356 (39.5)	125 (38.7)	231 (39.9)	0.7244					
B-blocker	769 (85.3)	277 (85.8)	492 (85.0)	0.7501					
Digoxin	270 (29.9)	115 (35.6)	155 (26.8)	0.0055					
Loop diuretics	743 (82.4)	253 (78.3)	490 (84.6)	0.0173					
Hydralazine	34 (3.8)	9 (2.8)	25 (4.3)	0.2469					
Nitrates	179 (19.8)	66 (20.4)	113 (19.5)	0.7406					
Statins	461(51.1)	131 (40.6)	330 (57.0)	<.0001					

ACEi: angiotensin converting enzyme inhibitor; ARB; angiotensin receptor blocker;

Appendix A

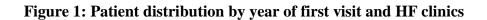
Recommended B-blockers

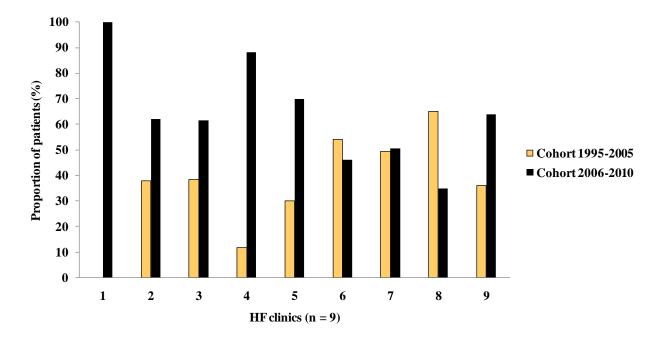
Medication	ChemicalName	Target dose	Dosing
Apo-Bisoprolol	bisoprolol fumarate	10	qdaily
Apo-Carvedilol	carvedilol	25	bid
Apo-Metoprolol	metoprolol tartrate	100	bid
Apo-Metoprolol Sr	metoprolol tartrate	100	bid
Apo-Metoprolol-L	metoprolol tartrate	100	bid
Betaloc	metoprolol tartrate	100	bid
Betaloc Durules	metoprolol tartrate	100	bid
Coreg	carvedilol	25	bid
Gen-Metoprolol	metoprolol tartrate	100	bid
Gen-Metoprolol (Type L)	metoprolol tartrate	100	bid
Lopresor	metoprolol tartrate	100	bid
Lopresor Sr	metoprolol tartrate	100	bid
Metoprolol	metoprolol tartrate	100	bid
Monocor	bisoprolol fumarate	10	qdaily
Novo-Bisoprolol	bisoprolol fumarate	10	qdaily
Novo-Carvedilol	carvedilol	25	bid
Novo-Metoprol	metoprolol tartrate	100	bid
Nu-Metop	metoprolol tartrate	100	bid
Pms-Bisoprolol	bisoprolol fumarate	10	qdaily
Pms-Carvedilol	carvedilol	25	bid
Pms-Metoprolol B	metoprolol tartrate	100	bid
Pms-Metoprolol-L	metoprolol tartrate	100	bid
Ran-Carvedilol	carvedilol	25	bid
Ratio-Carvedilol	carvedilol	25	bid
Sandoz Bisoprolol	bisoprolol fumarate	10	qdaily
Sandoz Metoprolol Sr	metoprolol tartrate	100	bid

Recommended ACE/ARB

Medication	ChemicalName	Target dose	Dosing
Accupril	quinapril hcl	20	bid
Accuretic	quinapril hcl & hydrochlorothiazide	40	qdaily
Altace	ramipril	10	qdaily
Altace Hct	ramipril & hydrochlorothiazise	10	qdaily
Apo-Capto	captopril	25-50	tid
Apo-Enalapril	enalapril maleate	10	bid
Apo-Fosinopril	fosinopril sodium	20	qdaily
Apo-Lisinopril	lisinopril	20-35	qdaily
Apo-Lisinopril/Hctz	lisinopril & hydrochlorothiazide	20-35	qdaily
Apo-Ramipril	ramipril	10	qdaily
Atacand	candesartan cilexetil	32	qdaily
Atacand Plus	candesartan cilexetil & hydrochlorothiazide	32	qdaily
candesartan	candesartan	32	qdaily
Capoten	captopril	25-50	tid
Captopril	captopril	25-50	tid
Captril	captopril	25-50	tid
Co Enalapril	enalapril sodium	10	bid
Co Lisinopril	lisinopril	20-35	qdaily
Co Ramipril	ramipril	10	qdaily
conversyl	quinapril hel	40	qdaily
Coversyl	perindopril erbumine	8	qdaily
Coversyl Plus	perindopril erbumine & indapamide	8	qdaily
Coversyl Plus Ld	perindopril erbumine & indapamide	8	qdaily
Cozaar	losartan potassium	50	qdaily
Diovan	valsartan	160	bid
Diovan-Hct	valsartan & hydrochlorothiazide	160	bid
Gen-Captopril	captopril	25-50	tid
Gen-Enalapril	enalapril sodium	10	bid
Gen-Fosinopril	fosinopril sodium	20	qdaily
Gen-Lisinopril	lisinopril	20-35	qdaily
Gen-Lisinopril/Hctz	lisinopril & hydrochlorothiazide	20-35	qdaily
Gen-Ramipril	ramipril	10	qdaily
Hyzaar	losartan potassium & hydrochlorothiazide	50	qdaily
Hyzaar Ds	losartan potassium & hydrochlorothiazide	50	qdaily
Lin-Fosinopril	fosinopril sodium	20	qdaily
losartan	losartan	50	qdaily

Mavik	trandolapril	4	qdaily
Monopril	fosinopril sodium	20	qdaily
Nov-Enalapril	enalapril sodium	10	bid
Novo-Captoril	captopril	25-50	tid
Novo-Enalapril	enalapril sodium	10	bid
Novo-Fosinopril	fosinopril sodium	20	qdaily
Novo-Lisinopril P	lisinopril	20-35	qdaily
Novo-Lisinopril Z	lisinopril	20-35	qdaily
Novo-Lisinopril/Hctz Type P	lisinopril & hydrochlorothiazide	20-35	qdaily
Novo-Lisinopril/Hctz Type Z	lisinopril & hydrochlorothiazide	20-35	qdaily
Novo-Ramipril	ramipril	10	qdaily
Nu-Capto	captopril	25-50	tid
perindopril	perindopril	8	qdaily
Pms-Captopril	captopril	25-50	tid
Pms-Enalapril	enalapril sodium	10	bid
Pms-Fosinopril	fosinopril sodium	20	qdaily
Pms-Lisinopril	lisinopril	20-35	qdaily
Prinivil	lisinopril	20-35	qdaily
Prinzide	lisinopril & hydrochlorothiazide	20-35	qdaily
quinapril	quinapril	40	qdaily
Ramipril	ramipril	10	qdaily
Ran-Lisinopril	lisinopril	20-35	qdaily
Ratio-Captopril	captopril	25-50	tid
Ratio-Enalapril	enalapril sodium	10	bid
Ratio-Fosinopril	fosinopril sodium	20	qdaily
Ratio-Lisinopril P	lisinopril	20-35	qdaily
Ratio-Lisinopril Z	lisinopril	20-35	qdaily
Ratio-Ramipril	ramipril	10	qdaily
Sandoz Enalapril	enalapril sodium	10	bid
Sandoz Lisinopril	lisinopril	20-35	qdaily
Sandoz Lisinopril/Hct	lisinopril & hydrochlorothiazide	20-35	qdaily
Sandoz Ramipril	ramipril	10	qdaily
Taro-Enalapril	enalapril sodium	10	bid
valsartan	valsartan	160	bid
Vasotec	enalapril sodium	10	bid
Zestoretic	lisinopril & hydrochlorothiazide	20-35	qdaily
Zestril	lisinopril	20-35	qdaily





Chapter 4: Effectiveness and economic evaluation of multi-disciplinary heart failure clinics: a population based study

Objective

The objective of Phase 4 was to compare clinical effectiveness and health care costs for the cohort of Ontario patients treated at specialized HF clinics to a cohort of HF patients treated with standard care. In addition, we evaluated which characteristics of HF clinic service models were predictive of improved outcomes.

Methods

Research Ethics Board Approval

This study was approved by the Institutional Research Ethics Board at Sunnybrook Health Sciences Centre, Toronto, Ontario.

Data Sources

This analysis utilized population-based administrative databases at the Institute for Clinical Evaluative Sciences (ICES). These databases were linked using encrypted unique patient identifiers thereby protecting patient confidentially, while allowing for the longitudinal evaluation of clinical and economic outcomes. The Canadian Institute for Health Information discharge abstract database (CIHI-DAD) has records on the frequency and type of all acute and chronic care hospitalizations in the patients included in our cohort. The CIHI discharge record includes a 'most responsible' diagnosis and up to 15 additional diagnosis codes that can be used to estimate co-morbidity, as well as procedure codes, length of stay and inhospital mortality data. The Ontario Registered Persons Database was used to ascertain mortality outcomes. National Ambulatory Care Reporting Service (NACRS) database contains administrative, clinical, financial, and demographic data for hospital-based ambulatory care, including emergency department visits, outpatient surgical procedures, medical day/night care, and high-cost ambulatory clinics such as dialysis, cardiac catheterization, and oncology(22). Data on physician visits and laboratory tests were obtained from the claims history in Ontario Health Insurance program (OHIP) database, which includes fee-for-service claims submitted by physicians and other licensed health professionals(22).

Finally, data on HF medication were obtained from the Ontario Drug Database (ODB), which has comprehensive drug utilization information on patients over 65 years, for whom full drug coverage is provided for by the MOHLTC(22).

Study Design and Sample

We performed a prospective cohort study of patients discharged alive after an acute care hospitalization for HF in fiscal year 2006 (April 1st, 2006-March 31st 2007), comparing patients treated in HF clinics to a matched HF cohort treated with standard care. Patients were identified based on International Classification of Disease (ICD) Version 10 code I50 in the CIHI-DAD. We restricted the cohort to patients above the age of 20 years who were residents of Ontario with valid Ontario Health Insurance Plan (OHIP) identification numbers. For patients who had more than one HF hospitalization in 2006, we defined the first hospitalization as the index event. The overall schematic for the study design is shown in Figure 1.

We categorized patients as either HF clinic patients or standard care patients based on the presence of an OHIP claim, with a principal diagnosis of HF, by one of 91 identified HF clinic physicians, within 1 year of the index event. HF clinic physicians were identified in a separate study, in which an environmental scan of the specialized multidisciplinary clinics across the province of Ontario was performed (Phase 1 and 2). In addition to obtaining billing numbers of HF clinic physicians, this environmental scan involved the use of a validated instrument to characterize the intensity and complexity of the

service model at each clinic. The HF Disease Management Scoring Instrument (HF-DMSI) developed by Riegel and colleagues describes the clinics across 10 categories (see Appendix 1). As a supplement to the information provided by the HF-DMSI, using concept mapping, an expert panel categorized the 23 specialized HF clinics in fiscal year 2006 into one of 3 strata (high, medium, and low) of clinic intensity (see Chapter 2 for details).

Of the 91 HF clinic physicians in practise in 2006-2007 in Ontario, only 74 (81%) consented to having their OHIP billing numbers used in this study. To mitigate the potential of misclassification of HF clinic and standard care patients, we excluded all patients discharged from a hospital in which any of the non-consenting HF clinic physicians practised (please see Appendix 2 for list of excluded institutions).

Outcomes

The primary effectiveness outcome of interest was all-cause mortality, determined from the Ontario Registered Persons Database. Secondary outcomes were all-cause hospitalization, and hospitalization for HF, based on the CIHI-DAD. In addition, we estimated cumulative cost, adjusted to 2010 Canadian dollars as an economic outcome. The perspective of the economic analysis was that of the Ontario Ministry of Health and MOHLTC, the single third party payer for health services in the province. Please see Appendix 3 for a detailled description of the cost estimation using administrative databases.

Statistical Analyses

A. Propensity Match

As this is an observational study, we anticipated that the study cohorts would have substantial differences in important covariates. To adjust for this, we used propensity score matching. Propensity score analysis has become a popular analytical method to balance the influence of measured confounding factors.(23;24) Briefly, we fitted a logistic regression model, with the dependent variable (ie exposure) being seen in a specialized HF clinic (dichotomous variable). All potential covariates that could be predictive of mortality in HF patients were included in the model (25). Covariates of interest were obtained using administrative databases, using the most recent index HF hospitalization in the look-back window. A summary of the administrative databases used, and the covariates definitions are provided in Appendix 4.

A propensity score of the predicted probability of being seen in a specialized HF clinic was calculated using this model. We then created a propensityscore-matched cohort by attempting to match each patient in the HF clinic cohort with one in the control cohort (a 1:1 match).(23;24) A nearestneighbour-matching algorithm was used to match patients on the basis of the logit of their propensity score, with matching occurring if the difference in the logit of the propensity scores was less than 0.2 times the standard deviation of the scores (the caliper width).(23;24) In 'greedy nearest-neighbour matching', a study cohort patient was randomly selected and matching was attempted with the "nearest" standard cohort patient.(23;24) This process was

repeated until matches are found for all patients in the HF clinic cohort.(23;24) Each matched pair was unique, and data for unmatched patients in either cohort were not used in subsequent analyses. Standardized differences of the mean (< 0.1) were used to indicate good balance in the matched sample.(23;24)

B. Clinical Outcomes

Kaplan-Meier survival curves for each primary and secondary outcome were constructed for the matched study and control cohorts.(24) These were compared using survival analysis techniques, adjusted for matched data.(24)

To explore the characteristics of HF clinics that are associated with improved outcomes, Cox-proportional hazard models were developed. In these models, the population of interest was restricted to the HF clinic population. The models were hierarchical, with clustering by clinic. We created separate models with all-cause mortality, allcause hospitalization and HF hospitalization as the dependent variable. After adjustment for patientlevel co-morbidities, the co-variates of interest were the scores on the HF-DMSI instrument, and the clinic intensity strata. The HF-DMSI scores were treated as ordinal variables. We first evaluated each HF-DMSI category individually. The final model included only HF-DMSI categories that were statistically significant when evaluated individually.

C. Economic Outcomes

The mean 3 year cumulative costs were estimated for each cohort. Although follow-up was complete up to March 31st, 2010, because cases and controls

were accrued over the course of fiscal year 2006, there were staggered follow-up dates. To avoid the issues of costs with censoring, we calculated cumulative costs up to death or the minimum full follow-up period for surviving patients. A 2-sample linear regression model for matched samples, was used to assess differences between the standard and study cohorts.(26;27)

To calculate the cost effectiveness of HF clinics, we determined the incremental cost-effectiveness ratio (ICER), calculated as the incremental cost per life year gained. The life-expectancy was calculated as the area under the Kaplan-Meier curves constructed for the HF clinic and standard care cohorts. The time-horizon for the cost effectiveness analysis was the minimum follow-up period for surviving patients as defined above. The costs and health outcomes were not discounted.

Sensitivity Analyses

LV function

Because this propensity match uses only covariates from administrative databases, it was important to ensure that important clinical variables were also well matched. Specifically, we wished to evaluate the degree to which the above algorithm would match for left ventricular (LV) function. LV function is an important prognostic predictor, with studies showing that HF patients with persevered LV function (ie LV function > 45%) have improved survival compared to patients with reduced LV function. LV function data is not found in administrative databases. To test the degree to which our propensity match balanced LV function between HF clinic and standard care patients, we repeated the above propensity score in a separate cohort from the Enhanced Feedback for

Effective Cardiac Treatment (EFFECT) study, with both administrative data and clinical data on LV function. The EFFECT study was a chart abstraction of 9,943 HF patients, across 44 hospitals in Ontario followed for up to 12 years (28).

Survivorship Bias

The definition of HF clinic patients in our study necessitated that a patient discharged alive after a HF hospitalization survived until a HF clinic physician saw them. We performed two landmark analyses, first restricting our analysis to patients who survived at least 1 year after discharge from the index event, and second, restricting it to patients who survived at least 30 days post-discharge, to evaluate the impact of survivorship bias on our conclusions. After 1 year, all HF clinic patients had been seen in clinic, while at 30 days, 50% of HF clinic patients had been seen.

Stratified Economic Analyses

In a post-hoc analysis, we repeated the economic analyses, calculating ICERs comparing high, medium or low intensity clinics to standard care. For each of these intensity strata, the propensity score was recalculated, with the exposure variable for the logistic regression being high/medium/low intensity clinics, and the match redone.

All analyses for clinical outcomes and health related costs were performed using SAS Version 9.1 (SAS Institute). The cost-effectiveness analysis model was conducted in Microsoft Excel (Version 2007). A two-sided p-value of 0.05 was considered significant.

Results

Study Sample

From April 2006 to March 2007, 16,300 patients were admitted to hospital with a primary diagnosis of HF. When restricted to patients over the age of 20, with valid Ontario health card numbers and to patients who survived until discharge, our sample size was 14,468. Of these patients, 1,288 were seen by HF clinic physicians within 1 year of their index discharge. These patients were seen at 21 different HF clinics, spread across the province. 2,184 patients were excluded (13% of overall group) because they were discharged from institutions in which we had incomplete HF physician billing data, and therefore could not be accurately classified. As illustrated in Figure 2, we had a final HF clinic cohort of 1,288 and 10,996 standard care patients.

Baseline Characteristics

Prior to matching, these two cohorts were substantially different (see Appendix 5). Patients in HF clinics tended to be younger, with a mean age of 71.8 years (standard deviation [SD] 13.4), compared to 77.0 years (SD 11.5) for standard care patients. More males (60.1% vs. 47.9%) were seen in HF clinics. There were substantial difference in residence and socioeconomic status, with more urban (92.5% vs. 80.9%), wealthy patients in HF clinics, and in general, standard care patients had more co-morbidities.

In Table 1, the baseline characteristics of HF clinic and standard care patients after propensity matching is shown. All 1,288 HF were successfully matched to standard care patients. There was good balance between the two groups with standardized differences less than 0.1.

There was complete follow-up until March 31st, 2010 for all patients. The minimum follow-up for surviving patients in our cohort was 1076 days.

Clinical Outcomes

Over the 4 years of follow-up, all-cause mortality was 52.1% in the HF clinic cohorts compared to 54.7% in the standard care group, which was statistically significant, with a p-value of 0.02 (Figure 3, Table 2). In contrast, the HF clinic group has greater rates of both all-cause hospitalization (87.4% vs. 86.6%; p-value 0.009) and HF hospitalization (58.7% vs. 47.3%; p-value <0.001) in comparison to the standard care patients.

In Table 2, clinical outcomes for the stratified analysis are shown, comparing high, medium and low intensity clinics to propensity matched standard care patients. The statistically significant improved survival associated with HF clinics was observed in all three strata. In contrast, the higher rates of all-cause and HF hospitalization were observed only in the medium and low strata clinics.

Predictors of Improved Outcome

The 1,288 HF clinic patients were seen at 21 HF clinics, of which 8 were classified as high intensity clinics, 8 medium intensity clinics and 5 as low intensity clinics, based on a concept mapping exercise by an expert panel. The intensity and complexity of these clinics were evaluated using the HF-DMSI, across 10 categories, as summarized in Appendix 6. The high and medium intensity clinics had more comprehensive education and medication management programs, and

were more multi-disciplinary compared to low intensity clinics.

The relationship of these clinic level characteristics and patient outcomes is shown in Table 3. The results of the hierarchical Cox-proportional hazards model show differential impact of clinic intensity on death and hospitalization. More intense clinics had lower mortality (hazard ratio [HR] 0.7 (95% confidence interval [CI] 0.54-0.92; p-value 0.011;) in comparison to low intensity clinics. HF clinics that included the caregiver were associated with improved survival, as were clinics with peer support as an important component of the intervention (Table 3). Higher intensity clinics with multiple contacts between providers and patients of significant duration had a significant reduction in mortality (HR 0.17; 95% CI 0.11-0.27; p-value <0.0001) compared to clinics with only a single contact with little or no follow-up.

In contrast, more intense clinics were associated with higher rates of both all-cause hospitalization (HR 2.05; 95% CI 1.49-2.82; p-value <0.001) and HF hospitalization (HR 1.51; 95% CI 1.08-2.10; p-value 0.015). A more intensive medication management program was associated with reduced all cause and HF hospitalization (HR 0.28 and HR 0.37 respectively). However, greater involvement of caregivers, or a more comprehensive education program on supporting self care was associated with increased hospitalization (Table 3).

Economic Outcomes

Over the 1076 days of complete followup, the mean cumulative cost for a HF clinic patient was \$54,311 compared to \$39,994 for a standard care patient (p value <0.001). The increased costs associated with HF clinic patients were predominantly due to increased hospitalization costs (\$36,936 for HF clinic vs. \$26,868 for standard care; p-value <0.001). Nonetheless, the HF clinic patients had greater costs for all cost categories, including physician claims (\$10,780 vs. \$8452), emergency room visits (\$2,785 vs. \$2,361), same day surgery (\$2,526 vs \$1,218) and HF medication costs (\$1,283 vs \$1,094).

When costs were analyzed by clinic strata, in contrast to the overall results, there was no difference in cost between the high strata HF clinics and standard care (\$40,023 vs \$40,264). Both medium and low strata HF clinics continued to have statistically significantly higher costs. The costs and respective ICERS are found in Table 2. For the overall cohort, HF clinics had an ICER of \$158,344 per life year gained over the 3 years of follow-up. High intensity HF clinics dominated standard care, with lower costs and improved survival. The ICERS for medium and low strata clinics were \$220,397 and \$88,313 per life year gained respectively.

Sensitivity Analyses

1. Quality of matching between cases and controls-

Probably the single most important prognostic variable among heart failure patients is LVEF. Information about ventricular function is not available in administrative databases. In order to determine whether our covariate matching had resulted in a good match with respect to LVEF, we applied our matching algorithm to the EFFECT study cohort, a group for whom LVEF data are available (see Appendix 7). Although a good match was possible in the administrative co-variates used in our main analysis, there was imbalance

between LVEF between HF clinic patients and standard care patients. More patients with preserved LVEF were in the standard care group (22.5% vs 16.7%).

2.Landmark

The results of the landmark analyses, restricted to patients who survived at least 1 year or 30 days respectively after the index discharge is found in Appendix 8. In both analyses, there was no statistically significant difference between survival in the HF clinic group and the standard care group (1 year: 37.9% vs 39.1%; p-value 0.683; 30 days: 51.2% vs 53.9%; p-value 0.48).

Discussion

In this population-based comparison of HF patients treated at specialized HF clinics versus standard care, after a HF hospitalization, we found that only approximately 10% of HF patients are seen at specialized HF clinics after discharge with a HF hospitalization. Treatment at HF clinics was associated with a statistically significant reduction in mortality, but also a significant increase in both all-cause and HF hospitalizations, over 3 years.

HF clinics have been studied extensively in the literature as a preferred mode of ambulatory care delivery to patients with this complex condition. Meta-analyses of randomized controlled trials have generally shown that these clinics are associated with an improvement in mortality, with most also showing an improvement in hospitalization when compared to standard care (1;3;6;7;15-18;20;29-37).

In our population level analyses, we found similar improvements in mortality associated with HF clinics, albeit of a smaller magnitude, as would be expected in a real-world setting as opposed to that of a clinical trial (3;18). However, we found a statistically significant increase in both all-cause and HF-specific hospitalizations, unlike that seen in some randomized controlled trials (18). There are several potential explanations for our findings.

As ours is an observational study there is the possibility that the HF clinic cohort is systematically different that than the standard care group. We have used advanced contemporary statistical methods to mitigate this, but cannot rule out the possibility of persistent confounders (23). Nonetheless, as seen in our study and others, patients seen in specialized HF clinics tend to be younger, with less co-morbidity. As such, it is unlikely that an increase in hospitalization can be attributed solely to residual confounding.

Most importantly, the clinics evaluated in our field evaluation may not be representative of those evaluated in clinical trials. Indeed, in our previous work, we found a wide spectrum of service models. Notably, the HF clinics in Ontario are principally focused on outpatient care, with no in-hospital or home-based components. Several analyses suggest that hospital discharge planning, immediate post-discharge follow-up and a home-based intervention may be critical components of HF clinics, necessary in order to reduce hospitalizations (18;19).

The observational study design, with its large sample size affords the ability delve deeper into this possible explanation, and evaluate potential clinic-level characteristics that may contribute to these findings.

We found that higher intensity clinics, as determined by our expert panel were associated with decrease in mortality when compared to lower intensity clinics. The most important clinic level characteristic was the frequency and complexity of patients contact with the clinic. In addition, greater involvement of the patient's caregiver, and the presence of an integrated peer support program in the clinic were associated with improvements in mortality. Of note, intensity of medication management, and the

comprehensiveness of the education program did not appear to be a significant factor in reducing mortality, though medication management reduced hospitalization.

This finding is contrary to some of the prevailing hypothesis as to the mechanism of benefit of HF clinics. which suggest that HF clinics principally improved utilization and compliance of evidence-based medications. Instead, our results suggest that this model, though involvement of the caregiver and peer-support at higher intensity clinics, there is better screening and the potential for earlier intervention. While higher intensity clinics appeared to be associated with greater survival, these same clinics were associated with greater all-cause and HF-specific hospitalization. In this analysis, peersupport and care-giver involved, in addition to more comprehensive education was associated with more hospitalization, suggesting that the greater screening leads to earlier intervention that appears to be hospital based. Indeed, medication use, and high frequency of visits was the only factors associated with lower hospitalization.

These counter-intuitive findings provide new insight into the care of these patients in Ontario. They suggest that the mortality benefit afforded by HF clinics may be mediated in part by earlier hospitalization and intervention, and thus avoidance of critical deterioration. In this setting, one can argue that these hospitalizations are not avoidable, but maybe an important mediator of improved survival.

As seen in the economic evaluation, such hospitalizations are costly, with an

increased cost associated with HF clinic care, predominately driven by acute inhospital costs. The results of this economic evaluation differs from modelling work done by our group and others suggesting that HF clinics are cost-effective, when efficacy estimates derived from published randomized trials are employed (38-40).

Our previous work suggests that HF clinics in Ontario have a wide spectrum of service models, and as such the costeffectiveness of HF clinics may have important differences based on intensity. Given this heterogeneity in the HF clinics evaluated, a single overall economic evaluation may be misleading. Our stratified economic analysis reinforces this possibility, given the fact that high intensity clinics appear to be a dominant option. However, this analysis should be not be considered conclusive, as it was not pre-specified, and involved considerably fewer patients per intensity category.

Our study must be interpreted in the context of several limitations that merit discussion. First, as our analysis was limited to administrative data, we did not have information on LV function. As seen in our sensitivity analysis using the EFFECT database, the propensity match did not balance LV function, and it is likely that patients seen in HF clinics were more likely to have LV systolic dysfunction. The medications that are recommended for HF have proven efficacy in systolic dysfunction, and have not been shown to be beneficial in HF with preserved function. However, patients with preserved LV tend to have improved survival and less resource use; as such, this would suggest that we are underestimating the survival benefit

afforded by HF clinics in our main analysis.

A second important limitation is the method we used to classify HF clinic patients required physician billing numbers. This assumes that all HF patients seen by a HF clinic physician are seen in a HF clinic. This may not be true; nonetheless, it is likely that the care provided by a HF clinic physician to HF patients seen outside of a formal HF clinic is comparable to those in the HF clinic, mitigating this issue. In addition, we were not able to obtain all the billings numbers for HF clinic physicians as not all physicians consented. We addressed this issue by excluding all patients from institutions with incomplete billing information.

Finally, there is the potential for survivorship bias. In our sensitivity analysis, we address this using two landmark analysis. Due to the reduction in sample size, we no longer show a statistically significant improvement in mortality associated with HF clinics, as such, we cannot rule out the possibility of survivorship bias. Nonetheless, in both landmark analyses we continued to see a 2% absolute reduction in mortality with HF clinics, similar to our main analysis.

In conclusion, we found that HF clinics are associated with a robust improvement in mortality in patients discharged after a HF hospitalization, but an increase in hospitalizations. We believe this work will be of substantial value to policy makers in determining which features of a specialized HF clinic intervention are key in order to realize their beneficial effects on health outcomes.

Table 1: Baseline Characteristics of Matched Cohort

	HF Clinic	Non-HF clinic	Standardized difference (matched sample)	Standardized difference (original unmatched sample)
	N=1,288	N=1,288		_
Age (years, Mean \pm SD)	71.80 ± 13.35	71.65 ± 13.29	0.01	0.45
Male , N(%)	774 (60.1%)	823 (63.9%)	0.08	0.24
LHIN	= (0 = 0()	10 (0 00)	0.00	0.00
Missing	7 (0.5%)	10 (0.8%)	0.03	0.02
Erie St. Clair	9 (0.7%)	6 (0.5%)	0.03	0.3
South West	19 (1.5%)	25 (1.9%)	0.04	0.25
Waterloo Wellington	99 (7.7%)	103 (8.0%)	0.01	0.1
Hamilton Niagara Haldimand Brant	154 (12.0%)	168 (13.0%)	0.03	0.03
Central West	45 (3.5%)	50 (3.9%)	0.02	0.04
Mississauga Halton	102 (7.9%)	86 (6.7%)	0.05	0.38
Toronto Central	165 (12.8%)	168 (13.0%)	0.01	0.17
Central	177 (13.7%)	170 (13.2%)	0.02	0.17
Central East	205 (15.9%)	198 (15.4%)	0.01	0.18
South East	27 (2.1%)	31 (2.4%)	0.02	0.16
Champlain	192 (14.9%)	203 (15.8%)	0.02	0.16
North Simcoe Muskoka	71 (5.5%)	61 (4.7%)	0.04	0.04
North East	15 (1.2%)	9 (0.7%)	0.05	0.29
North West	<6 (0.1%)	0 (0.0%)	0.04	0.21
RIO				
Rural	95 (7.4%)	102 (7.9%)	0.02	0.3
Urban	1,192 (92.5%)	1,185 (92.0%)	0.02	0.3
Unknown	<6 (0.1%)	1 (0.1%)	0	0.01
Neighbourhood Income Equivalent				
1	272 (21.1%)	283 (22.0%)	0.02	0.11
2	277 (21.5%)	281 (21.8%)	0.01	0.01
3	225 (17.5%)	223 (17.3%)	0	0.05
4	252 (19.6%)	256 (19.9%)	0.01	0.06
5	256 (19.9%)	239 (18.6%)	0.03	0.13
Coronary artery disease	717 (55.7%)	734 (57.0%)	0.03	0.12
Old myocardial infarction	628 (48.8%)	613 (47.6%)	0.02	0.17
Diabetes mellitus	649 (50.4%)	662 (51.4%)	0.02	0.03
Hypertension	1,068 (82.9%)	1,039 (80.7%)	0.06	0.11
Cerebrovascular disease (Yes/No)	80 (6.2%)	74 (5.7%)	0.02	0.09
Chronic cerebrovascular disease	23 (1.8%)	25 (1.9%)	0.01	0.05
Chronic renal insufficiency	313 (24.3%)	323 (25.1%)	0.02	0

Chronic pulmonary disease	275 (21.4%)	276 (21.4%)	0	0.15
Dementia	43 (3.3%)	46 (3.6%)	0.01	0.15
Malignancy	76 (5.9%)	83 (6.4%)	0.02	0.06
Charlson Comorbidity Index				
<=2	539 (41.8%)	517 (40.1%)	0.03	0.04
2-3	260 (20.2%)	261 (20.3%)	0	0.01
3-5	329 (25.5%)	354 (27.5%)	0.04	0
> 5	160 (12.4%)	156 (12.1%)	0.01	0.06
Adjusted Clinical Group				
(ACG)				
<=3	440 (34.2%)	447 (34.7%)	0.01	0.04
3-5	313 (24.3%)	324 (25.2%)	0.02	0
5-8	314 (24.4%)	317 (24.6%)	0.01	0.03
> 9	221 (17.2%)	200 (15.5%)	0.04	0.02

Table 2: Clinical and Economic Outcomes

	Overall Cohort		High Strata		Medium Strata			Low Strata				
	HF clinic	standard	p-value	HF clinic	standard	p- value	HF clinic	standard	p-value	HF clinic	standard	p-value
n	12	288		36	55		48	37		3	364	
death	52.1%	54.7%	0.02	54.1%	65.6%	0.020	49.5%	55.8%	0.060	52.8%	67.7%	0.037
hospitalization	87.4%	86.6%	0.009	83.9%	91.1%	0.617	88.6%	82.3%	< 0.001	87.6%	84.6%	0.079
HF hospitalization	58.7%	47.3%	< 0.001	53.5%	47.2%	0.141	58.8%	39.0%	< 0.001	61.1%	45.3%	0.006
•												
Total cost	\$54,311	\$39,994	<.0001	\$40,023	\$40,264	0.94	\$54,947	\$34,119	<.0001	\$51,129	\$36,177	<.0001
ICER	\$158,344		dominates			\$220,397			\$88,313			

Table 3: Clinic Level Predictors of Outcome

Parameter	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
	DEATH		HF ADMISSION		ALL ADMISSION	
High Intensity	0.70(0.54,0.92)	0.0107	2.05(1.49,2.82)	< 0.0001	1.51(1.08,2.10)	0.015
Medium Intensity	y 0.56(0.39,0.80)	0.0015	2.71(1.82,4.03)	< 0.0001	1.83(1.23,2.73)	0.003
Low Intensity	Referent				Referent	
_			Recipient			
2	Referent		Referent		Referent	
3	0.67(0.50,0.88)	0.0048	2.35(1.67,3.32)	< 0.0001	1.94(1.45,2.60)	< 0.0001
4	0.76(0.63,0.93)	0.0068	2.22(1.74,2.82)	< 0.0001	1.92(1.57,2.36)	< 0.0001
Education and counseling aimed at supporting self-care						
1	Referent		Referent		Referent	
2	1.37(0.86,2.20)	0.188	2.12(1.25,3.59)	0.01	2.41(1.45,4.01)	7E-04
3	0.76(0.62,0.92)	0.0056	2.80(2.17,3.61)	< 0.0001	2.39(2.06,2.77)	< 0.0001
4	1.02(0.75,1.38)	0.9191	2.99(2.02,4.43)	< 0.0001	2.53(1.92,3.33)	< 0.0001
			Medication management			
2	Referent		Referent		Referent	
3	1.19(0.99,1.42)	0.0508	0.28(0.21,0.36)	< 0.0001	0.37(0.32,0.43)	< 0.0001
			Social support			
0	Referent		Referent		Referent	
1	0.73(0.59,0.89)	0.0021	0.82(0.64,1.06)	0.13	0.84(0.66,1.06)	0.146
2	0.82(0.68,0.99)	0.0436	1.10(0.86,1.40)	0.46	1.27(1.07,1.50)	0.006
			Complexity			
1	Referent		Referent		Referent	
2	0.12(0.07, 0.19)	< 0.0001	1.673(0.97,2.87)	0.07	0.97(0.62,1.51)	0.882
3	0.17(0.11,0.27)	<0.0001	0.95(0.59,1.53)	0.83	0.60(0.41,0.87)	0.007

Model adjusted for Charlson Comorbidity, Adjusted Clinical group, rurality index, income equivalent, hypertension, diabetes, malignancy, dementia, renal insufficiency, cererbrovascular disease, pulmonary disease, coronary disease, old myocardial infarction, age, gender,

Figure 1: Study Outline

Index Event Date: most recent HF hospitalization in 2006

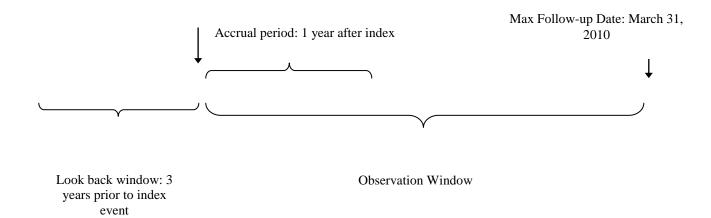


Figure 2

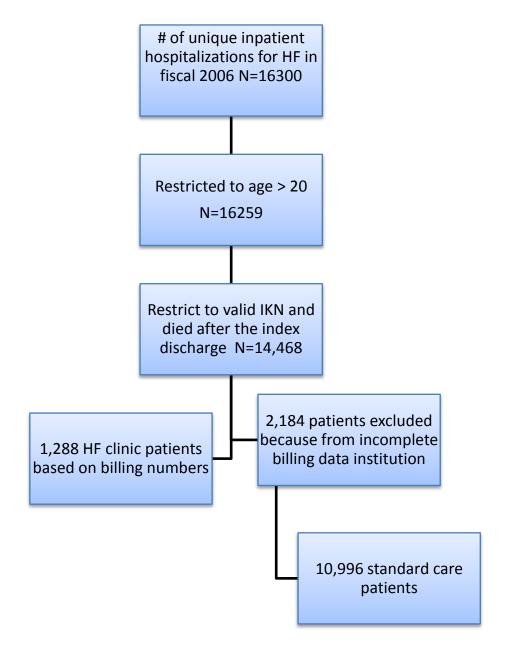
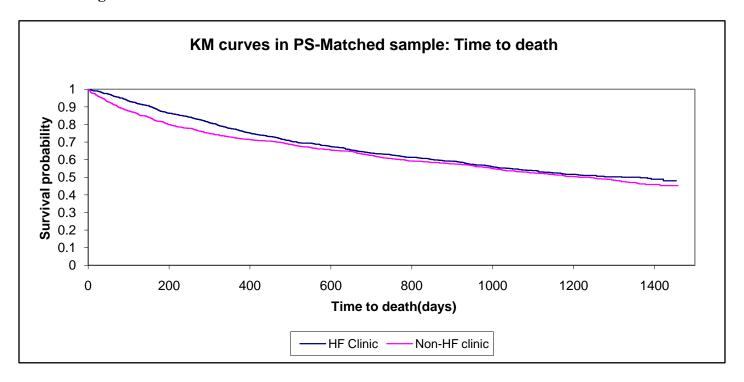
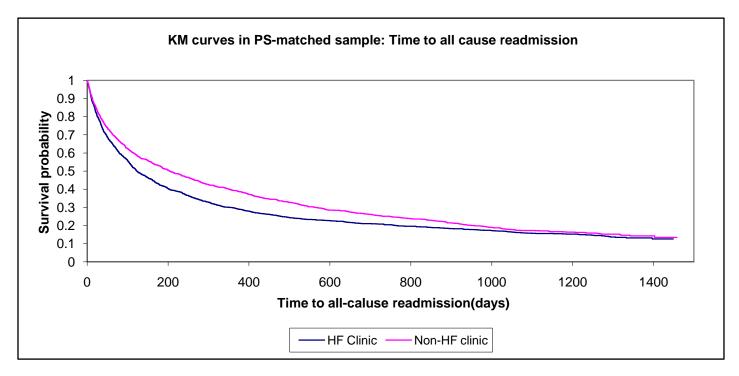


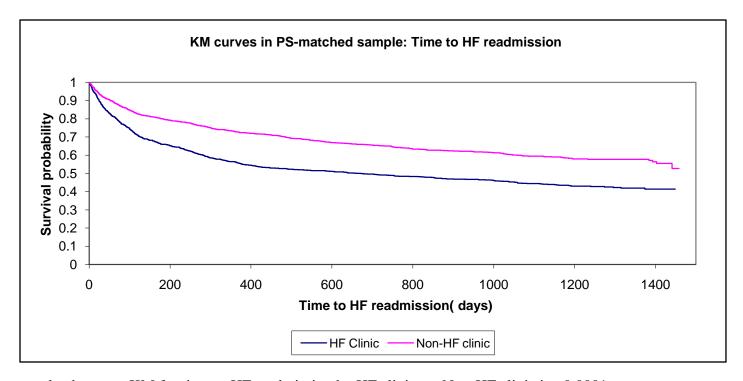
Figure 3



p-value between KM for time to death by HF clinic vs. Non-HF clinic is 0.02



p-value between KM for time to all-cause readmission by HF clinic vs. Non-HF clinic is 0.009



p-value between KM for time to HF readmission by HF clinic vs. Non-HF clinic is <0.0001

Appendix 1

Intervention category	Points to be assigned
	- Similar to 60 Managined
Recipient	1=Provider alone 2=Patient alone 3=Patient with some inclusion of caregiver 4=Patient with a caregiver who is central to the intervention
Intervention content	
Education and	0=No mention of education
counselling aimed at supporting self-care	1=Focus solely on importance of treatment adherence 2=Focus on treatment adherence including some creative methods of improving adherence
	3=Focus on surveillance but no mention of actions to be taken in response to symptoms (eg, no flexible diuretic management) 4=Emphasis on surveillance, management, and evaluation of symptoms in addition to
	treatment adherence
Medication management	0=No mention of medication regimen 1=Some mention of medications (eg, importance of medication compliance) but not an active part of the intervention. No attempt to intervene with provider to get patients on an evidence- based medication regimen
	2=Evidence-based medication regimen advocated but no follow-up with patient or provider to monitor the suggestion
	3=Medication regimen monitored, attempt made to get the patient on evidence-based medications, with follow-up monitoring done with patient or provider
Social support	0=No mention of a peer support intervention
Peer support	1=Peer support mentioned but not integral to intervention 2=Peer support integral component of intervention
Surveillance by provider:	0=No use of remote monitoring or telehealth 1=Remote monitoring is used in conjunction with other interventions that form the main intervention used
Remote monitoring	2=Telehealth is essential component of intervention
Delivery personnel	1=Single generalist provider (eg, physician, nurse, pharmacist) 2=Single HF expert provider (eg, physician, nurse, pharmacist) 3=Multidisciplinary intervention
Method of	1=Mechanized via internet or telephone
communication	2=Person-to-person by telephone
	3=Face-to-face, individual, or in a group
	4=Combined: Face-to-face at least once alone or in a
	group with individual telephone calls in between meetings
Intensity and complexity	
Duration	$1 = \le 1 \text{ mo}$ $2 = \le 3 \text{ mo}$ $3 = \le 6 \text{ mo}$ 4 = > 6 mo
Complexity	1=Low: single contact with little or no follow-up 2=Moderate: >1 but <4 and/or infrequent contact or contacts of short duration 3=High: multiple contacts of significant duration
Environment	1=Hospital: Inpatient only 2=Clinic/outpatient setting 3=Home-based
	4=Combination of settings

Appendix 2: Excluded Hospitals

Hospital Name:

London Health Sciences Center

Hamilton Health Sciences Corporation

Credit Valley

Trillium Health center

North York General

Ross Memorial

Appendix 3: Economic Outcomes

The primary economic outcome will be mean total cost/patient over the 3 years of follow-up (2007-2010). We will only include direct health care costs and the perspective of analysis is that of the Ministry of Health and Long Term Care of Ontario. Costs will be adjusted to 2010 Canadian dollars using the Consumer Price Index (CPI). Costs of interest include:

- 1. <u>Ambulatory Costs</u> (OHIP). OHIP claims are classified into:

 a. FP/GP visits, b. Specialist visits, c. Diagnostic tests, d. Other physician claims

 We used the median reimbursed (TOTPAID) amount for that fee code for that fiscal year for cost. For areas with shadow billing to record services provided through non-fee-for-service plans, the median (of non-zero TOTPAID) payment for all of the associated fee codes will be used for that fiscal year.
- Hospital admissions. Case mix group determined from CIHI-DAD to determine Resource Intensity Weight (RIW) for that year.
 Cost of hospitalization is RIW * cost per weighted case (CPWC) for that year.
 CPWC is published by the Ontario Joint Policy and Planning Committee (JPPC).
- 3. <u>ER visit</u>. Extracted all ER visits from CIHI National Ambulatory Care Reporting System (NACRS). Determine RIW weight from NACRS for that year. Cost is RIW * CPWC from JPPC.
- 4. **Day Surgery**: Apply same methodology as ER visit methodology using NACRS.
- 5. <u>Medications</u> (ODB), using only HF specific drugs, based on Drug Identification Numbers (DIN).

Appendix 4: List of Covariates

Variable	Source Database
Hospital type	insttype variable in CIHI record
Age (years)	Age at time of admission for index event (calculate using GETDEMO macro)
Gender (male/female)	Determine using GETDEMO macro
Residence (county)	County of residence (cnty) – determine using GETDEMO macro (option geodate = admdate) – also get cd variable using GETDEMO macro.
Residence (Local Health Integration Network)	Local Health Integration Network (1-14) of residence in CIHI discharge abstracts at time of index event
Hospital identifier (INST variable)	inst variable in CIHI discharge abstract
Hospital type	insttype variable in CIHI record
Rurality Index for Ontario (RIO) Neighbourhood Income Equivalent	Statistics Canada Postal Code Conversion file and Census data
Coronary artery disease (Yes/No)	ICD-10 codes I20 ; I21 ; I22 ; I24 ; I25 ; I513
Old myocardial infarction	ICD-10 code I25
Diabetes mellitus (Yes/No)	Presence in ODD 2007 database at any point before index event (prevyyyy ODD ≤ fiscal year of CIHI index event).
Hypertension (Yes/No)	Presence in Hypertension 2007 database any point before index event (diagdate ≤ index date for index event).
Cerebrovascular disease (Yes/No)	ICD-10 codes I60 – I68 ; I69 ; G45 ; G46 , H34 .
Chronic cerebrovascular disease	ICD-10 code I69
Chronic renal insufficiency (Yes/No)	(1) ICD-10 codes I12.0 ; I13.1 ; N03.2-N03.7 ; N05.2-N05.7 ; N18 ; N19 ; N25.0 ; Z49.0-Z49.2 ; Z94.0 ; Z99.2 .
Chronic pulmonary disease (Yes/No)	ICD-10 codes I27.8 ; I27.9 ; J40-J47 ; J60-J67 ; J68.4 ; J70.1 ; J70.3 .
Dementia (Yes/No)	ICD-10 codes F00 - F03; F05.1; G30; G31.1

Malignancy (Yes/No)				
– non-melanoma skin	ICD-10 codes: C00-26; C30-C34; C37-C41; C43; C45-C58;			
tumours excluded	C60-C85; C88; C90-C97.			
Charlson Comorbidity Index	Entire score.	Score. ICD-10 codes in CIHI discharge abstracts		
	Myocardial infarction	Yes/No. ICD-10 codes in CIHI discharge abstracts.		
	Congestive heart failure			
	Peripheral vascular disease			
	Cerebrovascular disease			
	Dementia			
	Chronic pulmonary disease			
	Rheumatologic disease			
	Peptic ulcer disease			
	Mild liver disease			
	Diabetes			
	Diabetes with chronic			
	complications			
	Hemiplegia or paraplegia			
	Renal disease			
	Any malignancy			
	Moderate to severe liver disease			
	Metastatic solid tumour			
	AIDS			
Adjusted Clinical Group (ACG)	ICD -10 codes from CIHI			

Appendix 5: Baseline Characteristics of Unmatched Cohorts

	HF Clinic	Non-HF clinic	p-vlaue
	N=1,288	N=10,996	
Age (years)			
Mean ± SD	71.80 ± 13.35	77.01 ± 11.47	<.001
male	774 (60.1%)	5,270 (47.9%)	<.001
LHIN			
Missing	7 (0.5%)	46 (0.4%)	<.001
Erie St. Clair	9 (0.7%)	944 (8.6%)	
South West	19 (1.5%)	863 (7.8%)	
Waterloo Wellington	99 (7.7%)	595 (5.4%)	
Hamilton Niagara Haldimand	154 (12.0%)	1,201 (10.9%)	
Brant			
Central West	45 (3.5%)	481 (4.4%)	
Mississauga Halton	102 (7.9%)	215 (2.0%)	
Toronto Central	165 (12.8%)	890 (8.1%)	
Central	177 (13.7%)	980 (8.9%)	
Central East	205 (15.9%)	1,125 (10.2%)	
South East	27 (2.1%)	629 (5.7%)	
Champlain	192 (14.9%)	1,103 (10.0%)	
North Simcoe Muskoka	71 (5.5%)	515 (4.7%)	
North East	15 (1.2%)	990 (9.0%)	
North West	<6 (0.1%)	419 (3.8%)	
RIO	0.5 (5.45)	• 00 = (10 0= ()	0.04
Rural	95 (7.4%)	2,086 (19.0%)	<.001
Urban	1,192 (92.5%)	8,898 (80.9%)	
Unknown	<6 (0.1%)	12 (0.1%)	
Neighbourhood Income			
Equivalent	272 (21 10/)	2.925 (25.79)	. 001
1	272 (21.1%)	2,825 (25.7%)	<.001
2	277 (21.5%)	2,408 (21.9%)	
3	225 (17.5%)	2,139 (19.5%)	
4 5	252 (19.6%) 256 (19.9%)	1,919 (17.5%) 1,664 (15.1%)	
	` ,	, , ,	
Missing	6 (0.5%)	41 (0.4%)	
Coronary artery disease (Yes/No)	717 (55.7%)	5,452 (49.6%)	<.001
•	` ′	4,462 (40.6%)	<.001
Old myocardial infarction	628 (48.8%)		
Diabetes mellitus (Yes/No)	649 (50.4%)	5,378 (48.9%)	0.315
Hypertension (Yes/No)	1,068 (82.9%)	9,532 (86.7%)	<.001
Cerebrovascular disease (Yes/No)	80 (6.2%)	975 (8.9%)	0.001
Chronic cerebrovascular disease	23 (1.8%)	288 (2.6%)	0.072
Chronic renal insufficiency (Yes/No)	313 (24.3%)	2,692 (24.5%)	0.887

Chronic pulmonary disease (Yes/No)	275 (21.4%)	3,064 (27.9%)	<.001
Dementia (Yes/No)	43 (3.3%)	781 (7.1%)	<.001
Malignancy (Yes/No) – non-	76 (5.9%)	813 (7.4%)	0.05
melanoma skin tumours excluded			
Charlson Comorbidity Index			
<=2	539 (41.8%)	4,396 (40.0%)	0.214
2-3	260 (20.2%)	2,193 (19.9%)	
3-5	329 (25.5%)	2,814 (25.6%)	
> 5	160 (12.4%)	1,593 (14.5%)	
Adjusted Clinical Group (ACG)			
<=3	440 (34.2%)	3,573 (32.5%)	0.604
3-5	313 (24.3%)	2,659 (24.2%)	
5-8	314 (24.4%)	2,805 (25.5%)	
> 9	221 (17.2%)	1,959 (17.8%)	

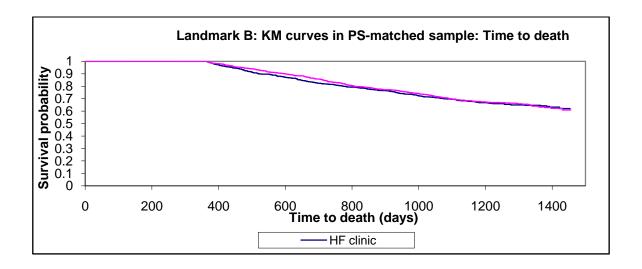
Appendix 6: Disease management interventions in heart failure clinics* (n = 21)

	Clinic intensity types All clinics				
HF-DMSI category	$(\mathbf{n} = 30)$	High	Medium	Low	
	$(\mathbf{H} = \mathbf{S}0)$	(n = 10)	(n = 13)	(n = 7)	p-value
Recipient	3.3±0.6	3.7±0.5	3.2±0.6	3.0±0.6	.040
Education and counselling	3.2±1.0	3.9±0.3	3.1±1.0	2.6±1.1	.011
aimed at supporting self-care					
Medication management	2.7±0.5	3.0±0	2.8±0.4	2.1±0.7	.002
Peer support	0.3±0.5	0.6±0.7	0.2±0.4	0.3±0.5	.147
Remote monitoring	0.7 ± 0.8	1.0±0.8	0.8 ± 0.8	0.1±0.4	.079
Delivery personnel	2.5±0.6	3.0±0	2.5±0.5	2.0±0.8	.002
Method of communication	3.6±0.5	4.0±0	3.5±0.5	3.4±0.5	.018
Duration	4.0±0	4.0±0	4.0±0	4.0±0	-
Complexity	2.6±0.6	3.0±0	2.6±0.5	2.0±0.6	<.001
Environment	2.0±0.2	2.0±0	1.9±0.3	2.0±0	.536

Appendix 7: EFFECT II HF cohort: Standardized Differences of baseline covariates in original and matched sample

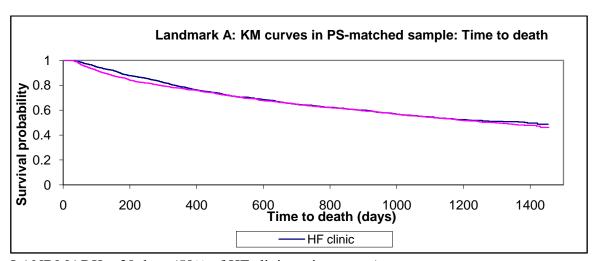
	HF Clinic	Non-HF clinic	Standardized difference (matched sample)	Standardized difference (original unmatched sample)
	N=621	N=621		
Age (years, Mean \pm SD)	72.88 ± 13.03	72.65 ± 12.45	0.02	0.3
Male, N(%)	337 (54.3%)	352 (56.7%)	0.05	0.1
LVEF				
<=45%	332 (53.5%)	251 (40.4%)	0.13	0.25
>45%	104 (16.7%)	140 (22.5%)	0.13	0.25

Appendix 8: Landmark Analysis



LANDMARK – 1 year days (all of HF clinic patients seen)

4 years	HF clinic	non-HF clinic	p-value
n	995		
death	37.9%	39.1%	0.64



LANDMARK – 30 days (50% of HF clinic patients seen)

4 years	HF Clinic	non-HF clinic	p-value
n	1,267		
death	51.2%	53.9%	0.48

Reference List

- (1) Arnold JM, Liu P, Demers C, Dorian P, Giannetti N, Haddad H, Heckman GA, Howlett JG, Ignaszewski A, Johnstone DE, Jong P, McKelvie RS, Moe GW, Parker JD, Rao V, Ross HJ, Sequeira EJ, Svendsen AM, Teo K, Tsuyuki RT, White M. Canadian Cardiovascular Society consensus conference recommendations on heart failure 2006: diagnosis and management. Can J Cardiol 2006; 22:23-45.
- (2) Johansen H, Strauss B, Arnold JM, Moe G, Liu P. On the rise: The current and projected future burden of congestive heart failure hospitalization in Canada. Can J Cardiol 2003; 19:430-5.
- (3) 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. J Am Coll Cardiol 2004; 44:810-9.
- (4) Komenda P, Levin A. Analysis of cardiovascular disease and kidney outcomes in multidisciplinary chronic kidney disease clinics: complex disease requires complex care models. Curr Opin Nephrol Hypertens 2006; 15:61-6.

- (5) Wright FC, De Vito C, Langer B, Hunter A. Multidisciplinary cancer conferences: a systematic review and development of practice standards. Eur J Cancer 2007; 43:1002-10.
- (6) Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW. 2009 Focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the International Society for Heart and Lung Transplantation. J Am Coll Cardiol 2009; 53:e1e90.
- (7) Medical Advisory Secretariat.
 Community-Based High
 Acuity Care for the
 Specialized Management of
 Heart Failure: an evidencebased analysis. Ontario
 Heath Technology Assessment
 Series 2009; 9.
- (8) Salganik MJ. Variance estimation, design effects, and

- sample size calculations for respondent-driven sampling. J Urban Health 2006; 83:i98-112.
- (9) Gustafsson L, Hodge A, Robinson M, McKenna K, Bower K. Information provision to clients with stroke and their carers: self-reported practices of occupational therapists. Aust Occup Ther J 2010; 57:190-6.
- (10) Gholizadeh L, Salamonson Y, Worrall-Carter L, DiGiacomo M, Davidson PM. Awareness and causal attributions of risk factors for heart disease among immigrant women living in Australia. J Womens Health (Larchmt) 2009; 18:1385-93.
- (11) Rankin J, Bhopal R.
 Understanding of heart disease and diabetes in a South Asian community: cross-sectional study testing the 'snowball' sample method. Public Health 2001; 115:253-60.
- (12) Riegel B, Lee CS, Sochalski J. Developing an instrument to measure heart failure disease management program intensity and complexity. Circ Cardiovasc Qual Outcomes 2010; 3:324-30.
- (13) Kelly G. The Psychology of Personal Constructs. 1955.
- (14) Rugg G, McGeorge P. The sorting techniques: a tutorial paper on card sorts, picture sorts and item sorts. Expert Systems 997; 14:80-93.

- (15) Albert NM, Fonarow GC,
 Yancy CW, Curtis AB, Stough
 WG, Gheorghiade M,
 Heywood JT, McBride M,
 Mehra MR, O'Connor CM,
 Reynolds D, Walsh MN.
 Outpatient cardiology practices
 with advanced practice nurses
 and physician assistants
 provide similar delivery of
 recommended therapies
 (findings from IMPROVE HF).
 Am J Cardiol 2010; 105:17739.
- (16) Gohler A, Januzzi JL, Worrell SS, Osterziel KJ, Gazelle GS, Dietz R, Siebert U. A systematic meta-analysis of the efficacy and heterogeneity of disease management programs in congestive heart failure. J Card Fail 2006; 12:554-67.
- (17) Gonseth J, Guallar-Castillon P, Banegas JR, Rodriguez-Artalejo F. The effectiveness of disease management programmes in reducing hospital re-admission in older patients with heart failure: a systematic review and meta-analysis of published reports. Eur Heart J 2004: 25:1570-95.
- (18) Holland R, Battersby J, Harvey I, Lenaghan E, Smith J, Hay L. Systematic review of multidisciplinary interventions in heart failure. Heart 2005; 91:899-906.
- (19) Phillips CO, Singa RM, Rubin HR, Jaarsma T. Complexity of program and clinical outcomes of heart failure disease management incorporating

- specialist nurse-led heart failure clinics. A metaregression analysis. Eur J Heart Fail 2005; 7:333-41.
- (20) Roccaforte R, Demers C, Baldassarre F, Teo KK, Yusuf S. Effectiveness of comprehensive disease management programmes in improving clinical outcomes in heart failure patients. A metaanalysis. Eur J Heart Fail 2005; 7:1133-44.
- (21) Ko DT, Mamdani M, Alter DA. Lipid-lowering therapy with statins in high-risk elderly patients: the treatment-risk paradox. JAMA 2004; 291:1864-70.
- (22) Jacobs P YR. Using
 Canadian administrative
 databases to derive
 economic data for health
 technology assessments.
 Ottawa: Canadian Agency for
 Drugs and Technologies in
 Health; 2009.
- (23) Austin PC, Mamdani MM, Stukel TA, Anderson GM, Tu JV. The use of the propensity score for estimating treatment effects: administrative versus clinical data. Stat Med 2005; 24:1563-78.
- (24) Tu JV, Bowen J, Chiu M, Ko DT, Austin PC, He Y, Hopkins R, Tarride JE, Blackhouse G, Lazzam C, Cohen EA, Goeree R. Effectiveness and safety of drug-eluting stents in Ontario.

- N Engl J Med 2007; 357:1393-402.
- (25) Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA 2003; 290:2581-7.
- (26) Bang H. Medical cost analysis: application to colorectal cancer data from the SEER Medicare database. Contemp Clin Trials 2005; 26:586-97.
- (27) Zhao H, Bang H, Wang H, Pfeifer PE. On the equivalence of some medical cost estimators with censored data. Stat Med 2007; 26:4520-30.
- (28) Ko DT, Alter DA, Austin PC, You JJ, Lee DS, Qiu F, Stukel TA, Tu JV. Life expectancy after an index hospitalization for patients with heart failure: a population-based study. Am Heart J 2008; 155:324-31.
- (29) Randomised trial of telephone intervention in chronic heart failure: DIAL trial. BMJ 2005; 331:425.
- (30) de la Porte PW, Lok DJ, van Veldhuisen DJ, van Wijngaarden J, Cornel JH, Zuithoff NP, Badings E, Hoes AW. Added value of a physician-and-nurse-directed heart failure clinic: results from the Deventer-Alkmaar heart failure study. Heart 2007; 93:819-25.

- (31) Del Sindaco D, Pulignano G, Minardi G, Apostoli A, Guerrieri L, Rotoloni M, Petri G, Fabrizi L, Caroselli A, Venusti R, Chiantera A, Giulivi A, Giovannini E, Leggio F. Two-year outcome of a prospective, controlled study of a disease management programme for elderly patients with heart failure.[see comment]. Journal of Cardiovascular Medicine 8(5):324-9, 2007.
- (32) Doughty RN, Wright SP, Pearl A, Walsh HJ, Muncaster S, Whalley GA, Gamble G, Sharpe N. Randomized, controlled trial of integrated heart failure management: The Auckland Heart Failure Management Study. Eur Heart J 2002; 23:139-46.
- (33) Dunagan WC, Littenberg B, Ewald GA, Jones CA, Emery VB, Waterman BM, Silverman DC, Rogers JG. Randomized trial of a nurse-administered, telephone-based disease management program for patients with heart failure. J Card Fail 2005; 11:358-65.
- (34) Mejhert M, Kahan T, Persson H, Edner M. Limited long term effects of a management programme for heart failure. Heart 2004; 90:1010-5.
- (35) Rao A, Walsh J. Impact of specialist care in patients with newly diagnosed heart failure: a randomised controlled study. Int J Cardiol 2007; 115:196-202.

- (36) Stromberg A, Martensson J, Fridlund B, Levin LA, Karlsson JE, Dahlstrom U. Nurse-led heart failure clinics improve survival and self-care behaviour in patients with heart failure: results from a prospective, randomised trial. Eur Heart J 2003; 24:1014-23.
- (37) Wierzchowiecki M, Poprawski K, Nowicka A, Kandziora M, Piatkowska A, Jankowiak M, Michalowicz B, Stawski W, Dziamska M, Kaszuba D, Szymanowska K, Michalski M. A new programme of multidisciplinary care for patients with heart failure in Poznan: one-year follow-up. Kardiol Pol 2006; 64:1063-70.
- (38) Capomolla S, Febo O, Ceresa M, Caporotondi A, Guazzotti G, La Rovere M, Ferrari M, Lenta F, Baldin S, Vaccarini C, Gnemmi M, Pinna G, Maestri R, Abelli P, Verdirosi S, Cobelli F. Cost/utility ratio in chronic heart failure: comparison between heart failure management program delivered by day-hospital and usual care.[see comment]. Journal of the American College of Cardiology 40(7):1259-66, 2002.
- (39) Miller G, Randolph S, Forkner E, Smith B, Galbreath AD. Long-term cost-effectiveness of disease management in systolic heart failure. Med Decis Making 2009; 29:325-33.

(40) Wijeysundera HC, Machado M, Wang X, van d, V, Sikich N, Witteman W, Tu JV, Lee DS, Goodman SG, Petrella R, O'Flaherty M, Capewell S, Krahn M. Cost-effectiveness of specialized multidisciplinary heart failure clinics in Ontario, Canada. Value Health 2010; 13:915-21.

Acknowledgments

THETA Cardiac Group:

- Harindra C. Wijeysundera (Lead Author)
- Gina Trubiani (Study Coordinator)
- Murray Krahn (Principal Investigator)
- Lusine Abrahamyan
- Luciano Ieraci
- Nicholas Mitsakakis
- Mike Paulden
- Anita Stern
- Gabrielle van der Velde
- William Witteman

Dr. Murray Krahn holds the F. Norman Hughes Chair in Pharmacoeconomics at the Faculty of Pharmacy, University of Toronto. This analysis was funded by funding provided to The Toronto Health Economics and Technology Assessment (THETA) Collaborative by the Ministry

of Health and Long-Term Care of Ontario (MOHLTC). The Institute for Clinical Evaluative Sciences (ICES) is funded in part by the MOHLTC. The funding organization did not have any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

We acknowledge and thank the contributions of all nurses, administrators and physicians at the participating HF Clinics, in addition to members of the steering committee and ICES advisory group.

Clinic name	MD	Nurse &
		Administrators
Cornwall Heart FailureClinic	P. De Young	M. Watt
Kitchener-St. Mary's Hospital	S. Smith	D. Lowry
	C. Rinne	
	G. Heckman	
Minto Mapleton-Family Health Team		V. LaForge
Credit Valley Hospital	H. Strauss	S. Tierney
	J. Cyriac	J. Burtcher
	S. Kremer	R. Gandhi
	M. Druck	
	J. Jovanovic	
	J. Nikhil	
	K. Nagi	
	M.Maingi	
Burlington Mememorial Hospital	B. Stevens	D. Weber
Hotel Dieu Hospital	J. McCans	P. Staples

		W. Earle
Picton-Prince Edward Family Health Team	P. Wattam	
University Health Network	H. Ross	L. Belford
	D. Delgado	
	P. Billia	
	P. Liu	S. Mohammad
Ottawa	H. Haddad	L. Clark
	L. Mielniczuk	
Trillium	A. Gupta	D. Button
	D. Harrison	
	P. Kannampuzha	
	T. Kalaparambath	
	M. Kirigin	
	C. Lazaam	
	C. LeFeuvre	
	G. Puley	
	T. Rebane	
	B. Sevitt	
	M. Platinov	
	I. Singh	
	R. Watson	
	S. Tishler	
	V. fluxar	
Orillia Soldier's Memorial Hospital	J. MacFadyen	D. Campbell
	S. Crewe	
	J. Jefferies	
	D. Bhatt	
Georgian Bay Family Health Team	E. Goode	G. Edwards
North York General Hospital	A. Cheng	J. Coldwell
	R. James	
	S. Klein	
	K. Kwok	
	B. Lubelsky	
	P. Myron	
	R. Rose	
	M. Strauss	
	Earl teitelbaum	I II 60
London Health Sciences Centre	P. Pflugfelder	J. Hoffman
London Health Sciences Centre	M. Arnold	A. Smith
Kitchener New Vision-Family Health Team	E M'II	A. Horton
Queensway-Carleton Hospital	F. Miller	J. Steele
	R. Grewal	

	T. McKibbin	
Lindsey, Ross Memorial	N. Krishnan	C. Follet
y ,	D. Kazhila	
Mt. Sinai Hospital	S. Mak	A. Schofield
	G. Newton	
	J. Parker	
	E. Azevedo	
Oakville Trafalgar Memorial Hospital	M. Heffernan	
Oukvine Trataigai Wemoriai Hospitai	J. Orfi	
	D. McConachie	
	R. Mao	
	V.	
	Chiamvimonvat	
	M. Feneck	
South Lake Regional	J. Symmmes	T. Fair
South Lake Regional	P. Hacker	L. Blair
	R. Chun	J. Allen
	M. Srivamadevan	J. Tillell
	J. Habot	
	M. Thangaroopan	
Scarborough-General Site	S. Roth	E. King
Scarborough-General Site	J Cherry	L. King
	E. Davies	
	A. Rosenbloom	
	G. Vertes	
	K. Yared	
Mt Forest		D. Hamizan
	K. Shelig	D. Horrigan A. Becks
Owen Sound-Grey Brice Health Sciences Center		A. Decks
Hamilton Health Sciences Center	R. McKelvie	L. Paul
St. Michael's Hospital	A. Al-Hesayen	D. Tuui
St. Michael's Hospital	G. Moe	
Toronto East General Hospital	V. Ovchinnikov	S. Garner
Sunnybrook Hospital	R. Myers	5. Guinei
Kitchener Center for family medicine	14. 141yo15	B. Ruby
Steering Committee		D. Ruoy
H. Abrams		
D. Alter		
M. DeMelo		
F. Wagner		
M. Parry		
K. Kingsbury		
K. Kiligsbury		

S. Tierney

M. Arnold

Institute for Clinical Evaluative Sciences (ICES) Advisory

J.V. Tu

P. Austin

X. Wang

Leslie Dan Pharmacy Building University of Toronto 6th Floor, Room 658 144 College Street Toronto, Ontario Canada M5S 3M2

T 416 946 3718

F 416 946 3719

E info@theta.utoronto.ca



www.theta.utoronto.ca