NOTE TO USERS

Université d'Ottawa · University of Ottawa

Université d'Ottawa · University of Ottawa

FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTDOCTORALES

FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES

Sophia PAPADAKIS

AUTEUR DE LA THÈSE - AUTHOR OF THESIS

Master in Health Administration

GRADE - DEGREE

MHA Program

FACULTÉ, ÉCOLE, DÉPARTEMENT - FACULTY, SCHOOL, DEPARTMENT

TITRE DE LA THÈSE - TITLE OF THE THESIS

Economic Evaluation of Cardiac Rehabilitation and Secondary Prevention Services

D. Angus

DIRECTEUR DE LA THÈSE - THESIS SUPERVISOR

CO-DIRECTEUR DE LA THÈSE - THESIS CO-SUPERVISOR

EXAMINATEURS DE LA THÈSE - THESIS EXAMINERS

D. Lane

G. Paquet

J.-M. De Koninck, Ph.D.

LE DOYEN DE LA FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTDOCTORALES

DEAN OF THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES

MASTER'S THESIS

Economic Evaluation of Cardiac Rehabilitation and Secondary Prevention Services

Sophia Papadakis[1]

Master's Thesis
Master in Health Administration
School of Management
University of Ottawa

Supervisors:
Douglas Angus, Health Economist[1]
Douglas Coyle, Health Economist[2]
Robert Reid, MBA, Ph.D.[3]

[1] Department of Health Administration, School of Management, University of Ottawa,
[2]Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa,
[3]University of Ottawa, and University of Ottawa Heart Institute Prevention and Rehabilitation Centre

April 10, 2004

Your file Votre référence
ISBN: 0-494-01572-1
Our file Notre référence
ISBN: 0-494-01572-1

Abstract

Little is known about the relative cost-effectiveness (CE) of different cardiac rehabilitation (CR) program designs and how CE is influenced by a patient's clinical and demographic characteristics. The aim of this study was to assess the 2-year incremental cost-utility of a distributed (12-month, 33 session) CR program to that of a standard (3-month, 33-session) CR program as assessed from the perspective of the cardiac health care system. 306 Patients (mean age=58.4 years, SD+/-9.7) with CAD were randomized to either standard or distributed CR. Program delivery costs, cardiac health care use, QALYS were tracked over a two-year period. The standard CR intervention was found to be dominant, resulting in both a cost saving and larger gains in QALYs in the 2-years following initiation of CR. Important differences were noted in CE of CR across cardiac risk strata and diagnosis groups, suggesting patients may benefit from triage to available CR models.

Acknowledgement

There are several people whose guidance and support have been invaluable to me in the completion of this Master's Thesis. I would like to thank Doug Angus for his mentorship throughout this process. Doug Coyle, I thank you for sharing your expertise in the area of health economics. I thank Dr. Neil Oldridge for his guidance and advise in the design, execution of this trial. It is with sincere appreciation that I recognize Dr. Robert Reid, Dr. William Dafoe, Ms. Louise Morrin, Ms.. Louise Beaton for their never ending support. Finally, I would like to thank my parents, family, and friends for their love and support.

Table of Contents

CHAPTER 3: COST UTILITY OF STANDARD VERSUS DISTRIBUTED CARDIAC REHABILITATION PROGRAM DELIVERY

EXECUTIVE SUMMARY

EXHIBITS, FIGURES AND TABLES

EXHIBITS

TABLES

FIGURES

EXECUTIVE SUMMARY

BACKGROUND: The growing number of aging Canadians and continuing constraints on health care resources accentuates the need to develop and disseminate cost-effective interventions for the prevention and management of cardiovascular disease. Exercise-based cardiac rehabilitation (CR) programs have been recognized as cost-effective interventions resulting in decreases in all-cause mortality, improvements in patient quality of life, and cardiac risk factors compared to standard care. Little is known about the relative cost-effectiveness of different cardiac rehabilitation program designs and how cost-effectiveness may be influenced by patient characteristics. The evaluation of alternative CR program delivery models will add to our understanding of how best to design and fund cardiac rehabilitation services to maximize outcomes for patients and the health care system.

OBJECTIVES: This Master's Thesis was designed as a three-part study with the following objectives:

(1) To summarize and evaluate published economic evaluations of cardiac rehabilitation programs and make recommendations regarding future directions;

(2) To compare in patients with Coronary Artery Disease (CAD) a 3-month (33-session) versus a 12-month (33-session) program of cardiac rehabilitation as measured one year following program intake for indices of cost effectiveness;
(3) To evaluate the comparability of utility scores derived through the TTO utility measure and SF-6D preference based index; and examine the implications of difference in utility scores on the calculation of quality adjusted life years and the cost-utility ratios of two competing cardiac rehabilitation interventions.

METHODS: Three linked stud methodologies were developed to meet the objectives as outlined. A systematic review of economic literature surrounding cardiac rehabilitation was conducted and an assessment of the methodological rigour of published studies was complete. Secondly, A prospective randomized control trial (RCT) comparing the cost utility of standard (3-month) CR program t a 12-month CR program over 2-years was complete. Finally a sub-study was complete using the RCT data set, which compared the time-trade-off direct utility measure to the newly developed SF-6D preference based utility index.

KEY FINDINGS: Seventeen trials were identified that were relevant to the economic evaluation of cardiac rehabilitation and secondary prevention services. Support for the cost-effectiveness and cost savings for health care systems of cardiac rehabilitation has been identified within this review. The body of literature supporting the cost-effectiveness of cardiac rehabilitation services is characterized by poor methodological quality. To date only one trial has provided a prospective randomized control trial evidence of the cost-effectiveness and cost-utility of supervised cardiac rehabilitation services.

The 3-month intervention was found to be dominant ($16,228/QALY), resulting in both a savings to the health care system and larger gains in QALYs over the 2-years following initiation of CRP. Stratified analyses suggest the standard 3-month program was a more cost-effective intervention for higher risk and CABG patients. The 12-month program was more cost-effective for lower risk patients and females. Important differences noted in the cost-effectiveness of CRP across cardiac risk strata and diagnosis groups, suggesting patients may benefit form triage to available CRP models.

Poor agreement was observed between utility scores derived from the SF-6D and Time-Trade-Off, suggesting differences in the underlying concepts they are measuring. Utility scores derived from the

SF-6D index displayed a larger distribution, while the TTO displayed a clustering of scores at the lower and upper end of the scale. This study supports the ability of the SF-6D to discriminate against small changes in the upper rage of the utility scale. The TTO and SF-6D were found to produce comparable mean QALY gains over the 2-year assessment period.

RELEVANCE: This study is the first full economic evaluation to evaluate alternative program delivery of cardiac rehabilitation services. This is also the first cost-utility analysis to utilize a broad based cardiac rehabilitation patient population. The study's findings will make a significant contribution to our knowledge about how best to design cost-effective cardiac rehabilitation interventions. The study has identified several recommendation and future research directions, which will add to the economic evaluation of cardiac rehabilitation services.

CHAPTER 1:
INTRODUCTION

Economic Evaluation of Cardiac Rehabilitation and Secondary Prevention Services

1.0 Introduction

1.1 Background

Coronary Artery Disease (CAD) is the leading cause of death and disability in Canada, accounting for more than 27% of deaths nation wide[1]. The total cost of CAD in 1993, the latest year for which this information is available, was $7.8 billion, which includes a direct cost of $2.1 billion and an indirect cost of $5.3 billion, making it the most expensive disease category within the Canadian Health Care system[1]. The growing number of aging Canadians and continuing constraints on health care resources accentuates the need to develop and disseminate cost-effective interventions for the prevention and management of cardiovascular disease.

Cardiac rehabilitation (CR) services are defined as comprehensive programs involving prescribed exercise, medical evaluation, education, counseling, and psychosocial support [2]. In patients with diagnosed CAD, exercise-based cardiac rehabilitation programs (CRPs) decrease mortality, improve exercise tolerance, and coronary risk levels[3]. Meta-analyses reviewing randomized, prospective studies of cardiac rehabilitation versus usual care, have confirmed its efficacy in reducing the chance of death after a heart attack by 20-25% [3-5]. Additionally, enhanced patient quality of life has emerged as an early benefit of CR services [6, 7]. As a result, secondary prevention through CR is recommended for all patients with coronary artery disease unless otherwise contraindicated [2].

The costs and relative benefits of delivering health care interventions has captured wide-spread attention [8, 9]. There is increasing demand for justification of health care expenditures and the development of interventions that will more effectively use our health care dollars.

Cardiac Rehabilitation services in particular have been scrutinized regarding the potential return on large program delivery investments and the challenge remains designing and evaluating available and emerging models for the delivery of cardiac rehabilitation services [10]. A variety of program models ranging from exercise only to multi-factorial programs have emerged, as well as, various delivery modes including individualized home-based and supervised group-based programs. Economic evaluation has emerged as an important tool in the evaluation of competing health care interventions and serves as a way to inform policy and more effectively allocate limited health care resources.

1.2 Thesis Design

This Master's Thesis was designed as a three-part study with the following objectives:

(1) To summarize and evaluate published economic evaluations of cardiac rehabilitation programs and make recommendations regarding future directions;

(2) To compare in patients with Coronary Artery Disease (CAD) a 3-month (33-session) versus a 12-month (33-session) program of cardiac rehabilitation as measured one year following program intake for indices of cost effectiveness;

(3) To evaluate the comparability of utility scores derived through the TTO utility measure and SF-6D preference based index; and examine the implications of difference in utility scores on the calculation of quality adjusted life years and the cost-utility ratios of two competing cardiac rehabilitation interventions.

The thesis objectives are presented as Chapters in this document. In Chapter 1 the results of the systemic review of economic literature surrounding cardiac rehabilitation is presented. In Chapter 2, a prospective randomized control trial of two alternative cardiac rehabilitation program models are compared in a cost-utility analysis In Chapter 3, we present a sub-study comparing to the time-trade-off direct utility measure to the newly developed SF-6D preference based utility index.

CHAPTER 2:
SYSTEMATIC REVIEW

Economic Evaluation of Cardiac Rehabilitation and Secondary Prevention Services

Executive Summary

Cost-effectiveness analysis has emerged as an important tool in the evaluation of health care practices and serves as a way to inform policy and more effectively allocate limited health care resources. The goal of this review is to summarize and evaluate published economic evaluations of cardiac rehabilitation programs and make recommendations regarding future directions.

Electronic databases (Medline 1966-2002, Polaris 1980-2002 and the Cochrane Effectiveness Practice Register) were searched for English language randomized control trials, non-randomized trials, modeling studies, and descriptive studies evaluating the economic impact of cardiac rehabilitation (secondary prevention of cardiovascular disease). Pre-standardized data abstraction forms were used to review the full texts of all potentially relevant articles. Publications were excluded if they were review articles, primary prevention, or unrelated to lifestyle change. Eligible studies were assessed for their strength of evidence using the Drummond criteria for economic evaluation.

Seventeen trials were identified that were relevant to the economic evaluation of cardiac rehabilitation and secondary prevention services. The search revealed 8 trials not included in previously published systematic reviews. Of the 17 studies included, 11 were cost analysis, 4 were cost-effectiveness analysis, 1 was a cost-description, 1 was a cost-minimization, and 1 was a cost-utility analysis. None of the trials reviewed met all of the Drummond checklist criteria adequately.

Support for the cost-effectiveness and cost savings for health care systems of cardiac rehabilitation has been identified within this review. The heterogeneity between study comparators, study designs, and perspectives makes pooling of study results inappropriate. The body of literature supporting the cost-effectiveness of cardiac rehabilitation services is characterized by poor methodological quality. To date only one trial has provided a prospective randomized control trial evidence of the cost-effectiveness and cost-utility of supervised cardiac rehabilitation services. Further trials are required to support the generalizability of these findings to the broader patient population. The literature evaluating home-based and alternative delivery models including the frequency and duration of cardiac rehabilitation is insufficient to draw conclusive recommendations regarding the cost-effectiveness of these delivery models.

The following recommendations are directed towards advancing policy and research surrounding the economic viability of cardiac rehabilitation.

- Greater dissemination of best practices in the design of economic evaluations is required within the field of cardiac rehabilitation.
- Well-designed trials evaluating the cost-effectiveness and cost-utility of supervised cardiac rehabilitation against standard are required to support the findings of Oldridge (1993).
- There is a need to expand the evidence base supporting the economic viability of cardiac rehabilitation to the broader cardiac population including women and other diagnosis groups.
- Initiate well-designed trials evaluating the cost-effectiveness and cost-utility of alternative CR delivery models including home-based rehabilitation programs, telephonic interventions, and specific delivery model characteristics.

2.1 BACKGROUND

2.1.1 Economic Evaluation

Two main categories of economic evaluation exist (See Table 2.1). Partial economic analyses are those analyses, which evaluate either the costs or consequences between two interventions or both the costs and consequences of a single intervention [11]. Full economic analyses are those analyses, which evaluate both the cost and consequences between two or more interventions. Full economic evaluations will provide a cost to consequence ratio (C/C ratio). Definitions for each type of partial and full economic evaluation are provided.

Table 2.1: Description of Economic Analysis Type

Analysis Type	Description
Partial Economic Evaluation	
Cost Description	An evaluation of the overall cost of a single intervention [12].
Cost-outcome Description	The evaluation reports both the cost and effects of a single intervention.
Cost Analysis	The evaluation reports costs but not effects of two or more comparators.
Full Economic Evaluation	
Cost-Minimization Analysis (CMA)	Evidence is available that the effectiveness of two or more interventions are equivalent, the analysis will therefore seek to identity the less costly intervention.
Cost-Effectiveness Analysis (CEA)	Cost-effectiveness is reported as a function of cost per unit of outcome. Consequences measured in natural units such as life years gained (LYG).
Cost-Utility Analysis (CUA)	Cost reported per Quality-Adjusted-Life Year (QALY). Consequences measured using a preference score (e.g. time-trade off) from which QALYs are estimated.
Cost-Benefit (CBA)	Both costs and health effects are given a monetary value [13].

2.1.2 Systematic Review

Systematic reviews are an approach to synthesizing and critically appraising existing evidence regarding a particular health issue [14]. The systematic review utilizes explicit and reproducible methods for identifying and selecting studies, and assessing each eligible study with respect to the strength of evidence it contains. Information from each study is extracted and evaluated against pre-established criteria. The systematic review allows a summary of research conducted to date to be generated and can assist in identifying areas where insufficient evidence exists, as well as, make recommendations for future research [14]. Systematic reviews are useful tools for evidence-based decision-making and development of practice guidelines [15].

The systematic review has gained wide acceptance within the health care field as one of the most valid methods for synthesizing accumulated evidence [16]. The number of systematic reviews published annually has increased 10-fold in the past decade [17-19]. Numerous guidelines have been published describing best practices for conducting systematic reviews [18, 20, 21]. While most systematic reviews have evaluated randomized controlled trials (RCTs), the same methods can be applied to the review of non-randomized trials particularly when few RCTs have been conducted [17, 22]. This systematic review has employed best practices based on available guidelines.

2.1.3 Previous Reviews

Several systematic reviews have been undertaken to evaluate the effectiveness of cardiac rehabilitation on clinical outcomes including morbidity, mortality, cardiac risk factors, and quality of life [3-5, 23]. Only two systematic reviews have looked at economic evaluations of cardiac rehabilitation services [13, 24].

A 1998 systematic review by Oldridge and colleagues summarized the body of literature regarding the economic evaluations of cardiac rehabilitation services [13]. The review identified 8 publications, which reported original data or findings on the cost-effectiveness of cardiac rehabilitation interventions (See Table 2.2). One described costs associated with program delivery, 1 was a cost-minimization analysis, 4 were cost analyses, and 2 were cost-effectiveness analysis, one of which was a randomized trial which also evaluated cost-utility.

The Canadian Coordinating Office of Health Technology Assessment (CCOHTA) initiated a systematic clinical and economic review of exercise-based cardiac rehabilitation programs in 2002 [24]. CCOHTA limited its review to full economic evaluations and cost studies evaluating exercise-based interventions against usual care published between 1995 and August 2001. Home-based CRP and comparisons between CR delivery models were not considered in the CCOHTA review. A total of 3 full economic evaluations and 3 cost studies were reviewed.

Table 2.2. Summary of 1998 Review by N.B. Oldridge [13]

Year	Author	Title	Type
1985	DeBusk et al. [25]	Medically directed at home cardiac rehabilitation soon after complicated acute myocardial infarction: a new model for patient care.	Cost-minimization
1991	Levin et. al. [26]	Cardiac Rehabilitation – a cost analysis	Cost analysis
1992	Ades et al. [27]	Cardiac rehabilitation participation predicts lower hospitalization costs	Cost analysis
1993	Edwards et. al [28]	Percutaneous transluminal coronary angioplasty rehabilitation: A cost-effective analysis	Cost analysis
1993	Oldridge et al. [29]	Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction	Cost-effectiveness / cost-utility
1995	Bondestam et. al. [30]	Effects of early rehabilitation on consumption of medical care during the first year after acute MI in patients >65 years of age	Cost analysis
1995	Allison et al. [31]	Medical and Economic costs of psychologic distress in patients with coronary artery disease	Cost description
1997	Ades et al. [32]	Cost-effectiveness of cardiac rehabilitation after MI	Cost-effectiveness

2.1.4 Methodological Quality

Several international guidelines for economic evaluation of pharmaceuticals and health technologies have been published [33-38]. Canadian guidelines have been jointly produced by academic institutions and government agencies since 1991 and most recently revised in 1999 [35, 36, 39, 40]. These documents provide descriptions of best practices involved in the measurement, costing, valuation, and analysis of economic evaluation of health care interventions. The US Public Health Services Panel on cost-effectiveness in health and medicine has published a "reference case" to guide the conduct of cost-effectiveness analysis

in an attempt to improve the quality and comparability of economic analyses [34]. The reference case summarizes the panel recommendations for the standard methods to be employed in cost-effectiveness analyses including; the use of a societal perspective, accounting of consequences (both harms and benefits), costs to all parties, the use of incremental comparisons, a fixed reference year, 3% discount rate, and at minimum, a univariate sensitivity analysis evaluating assumptions or estimates contained within the analysis.

Shephard (1992) published a critical study reviewing the economic literature surrounding secondary and tertiary cardiac rehabilitation [41]. This study determined seven weaknesses existed in the published literature at that time including: neglecting discount rate; a lack of consideration for opportunity costs; and the weakness of existing databases.

The methodological quality of economic evaluations included in the systematic review was assessed using the Drummond (1997) criteria for economic evaluations [11]. The ten-item criteria presented in Figure 2.1, is designed to provide a qualitative assessment of the strengths and weaknesses of published studies. Each of the criteria items assesses an important issue in the design of economic evaluations including: the assessment of all relevant costs and consequences, the use of a sensitivity analysis, the generalizability of the findings. Evaluators applying the criteria rank the study as meeting (yes) appraisal criteria, not meeting appraisal criteria (no), or can't tell (CT).

The Drummond criteria has been previously used in the evaluation of health care interventions [11, 42]. The criteria concur with the Canadian Guidelines for Health Technology Assessment and the U.S. Public Services Health Panel for economic evaluation [34, 36]. Michael Drummond is a well recognized expert in the field of health care economics and has lead several international tasks force in health economics including the Task Force on Use of Pharmacoeconomic/Health Economic Information in Health-Care Decision Making [43].

Figure 2.1: Drummond Checklist for Economic Appraisal

1. Was a well-defined question posed in an answerable form?
2. Was a comprehensive description of competing alternatives given?
3. Was there evidence that the programmes' effectiveness had been established?
4. Were all the important and relevant costs and consequences for each alternative identified?
5. Were costs and consequences measured accurately in appropriate physical units?
6. Were costs and consequences valued credibly?
7. Were the costs and consequences adjusted for differential timing? (Discounting)
8. Was an incremental analysis of costs and consequences of alternatives performed?
9. Was a sensitivity analysis performed?
10. Did the presentation and discussion of study results include all issues of concern to users?

2.2 Goals and Objectives

2.2.1 Goal

The goal of this review is to summarize and evaluate published economic evaluations of cardiac rehabilitation programs using the critical appraisal checklist developed by Drummond to assist with the assessing the validity of economic evaluations [11] and to make recommendations regarding future directions.

2.2.2 Objectives

The specific objectives of this review are:

(1) To identify and characterize the body of published literature evaluating economic aspects of cardiac rehabilitation for the secondary prevention of cardiovascular disease.

(2) To evaluate the methodological quality of the economic evaluations of cardiac rehabilitation programs/services published to date.

(3) To provide recommendations regarding future directions for economic evaluation of cardiac rehabilitation and secondary prevention services.

2.3 Methods

2.3 Search Strategy

2.3.1 Search Terms and Databases

Electronic databases (Medline 1966-2002, Polaris 1980-2002 and the Cochrane effectiveness practice register) were searched for English language randomized control trials, non-randomized trials, modeling studies, and descriptive studies evaluating the economic impact of cardiac rehabilitation (secondary prevention of cardiovascular disease). The following text word terms and MeSH headings were used: "Economic evaluation" or "costs" or "cost" or "cost-effectiveness" or "cost-benefit" or "cost-utility" and "cardiac rehabilitation" or "secondary prevention" or "lifestyle intervention". To identify additional studies, hand searches of bibliographies were conducted.

2.3.2 Selection of eligible studies

The titles and abstracts of all citations generated from the search were reviewed to identify any studies reporting on the economic evaluation of cardiac rehabilitation interventions. Pre-standardized data abstraction forms were used to review the full texts of all potentially relevant articles. Publications were excluded if they were review articles, primary prevention, or unrelated to lifestyle change. The review included partial economic evaluations, trials evaluating return to work, non-traditional cardiac rehabilitation interventions including home programs, community-based programs, and studies evaluating unique program delivery models.

2.3.3 Data Abstraction

A single independent reviewer completed the data extraction form (See Appendix 2). The abstraction form was utilized as the basis for data synthesis and evaluation. When necessary, authors were contacted to gain clarity regarding particular areas of the research publication.

2.3.4 Quality Assessment

Eligible studies were assessed for their strength of evidence using the Drummond Criteria for economic evaluation (See Appendix 4) [11]. The ten-item checklist was used as the basis for quality assessment of studies under review. Each study was ranked as meeting the criteria (yes), not meeting (no), or can't tell.

2.4 Results

2.4.1 Synthesis

Of the 352 citations originally identified using key word search combinations, a total of 291 were identified as potentially relevant upon abstract review. Sixty-one were excluded due to non-English publication type, 13 were review articles, 45 evaluated interventions that were did not evaluate cardiac rehabilitation populations, and 178 were found not to be economic investigations. Twenty-six studies were eligible for detailed review of which an additional 10 were excluded upon manuscript review because they did not evaluate economic outcomes. A total of 17 studies were identified as eligible for the present review. Table 2.3 provides an overview of the results of the of the search strategy. Exhibit 1 provides an overview of the 17 studies reviewed.

Table 2.3: Results for Identified Search Terms

Search Term	Results
Cost or Economic Evaluation	243,644
Cardiac Rehabilitation	1,579
Secondary Prevention of heart disease	2,856
Lifestyle Intervention	1,934
Combine all	352
English Language Only	291
Eligible following abstract review	26
Eligible for Systematic Review	17

2.4.2 Study Characteristics

The search revealed 8 trials not included in previously published systematic reviews. Six have been published since the 1998 Oldridge review and 2 had been excluded. Exhibit 2 and Exhibit 3 provide a summary of the study design and outcome measures for each of the studies evaluated. The majority of studies were published between 1991 and 2000. Of the 17 studies included, 11 were cost analysis, 4 were cost-effectiveness analysis, 1 was a cost-description, 1 was a cost-minimization, and 1 was a cost-utility analysis. The majority of the studies (58.8%) focused on the male Myocardial Infarction (MI) patient population. Forty-eight percent of the studies were conducted using RCT designs, 23.5% were nonrandomized trials, and 23.5% were modeling studies. The majority of studies conducted have utilized the perspective of the health care system with the primary outcome measure being re-hospitalization costs. Four of the studies included a societal perspective, and 4 studies included the patient perspective. Table 2.4 provided a breakdown of key study characteristics and more detailed overview is provided in Appendix 2.

Table 2.4: Methodological Overview (N=17)

	Articles	
	No.	%
Perspective		
Societal	5	29.4
Health Care System	9	52.9
Rehabilitation Program	3	17.6
Patient	4	23.5
Patient Population*		
Myocardial Infarction	10	93.8
Coronary Artery Bypass Graft (CABG)	5	31.3
Angioplasty (PTCA)	6	37.5
Combined	4	25.0
Heart Failure	1	5.9
CVD	14	100
Analysis Type		
Cost Description	1	5.9
Cost / Utilization Analysis	11	64.7
Cost Minimization	1	5.9
Cost Effectiveness	4	23.5
Cost Utility	1	5.9
Study Design		
Randomized Control Trial (RCT)	8	47.8
Non-Randomized	4	23.5
Modeling	4	23.5
Cohort Study	1	5.9

2.4.3 Comparative Evaluations

Four types of comparison were identified in the published literature. These include;

- Supervised CR vs. standard care [26, 27, 29, 30, 32, 44, 45];
- Home-based CR vs. standard care [30, 45, 46];
- Supervised CR vs. home-based CR [25, 45, 47];
- Comparison of two delivery formats / program components [28, 48-50].

Exhibit 3 provides a summary of the study design characteristics and findings for each of these comparison groupings. The findings for each of the comparison against standard care suggest positive outcomes favouring the intervention groups. Cost-analysis comparisons between supervised and non-supervised programs suggest that home-based programs are the more cost effective delivery model [25, 27, 32, 45, 47]. No full prospective economic analysis of non-supervised programs has been conducted to date. Trials evaluating delivery formats indicate that mode of delivery can play an important role in how resources are utilized to achieve a desired outcome.

2.4.4 Methodological Quality

Exhibit 6 provides a summary of the Drummond Reviews for all 17 studies included in this evaluation. The assessment criteria provide an evaluation of the methodological quality of the trials conducted. None of the trials reviewed met all of the checklist criteria adequately. Three of the 17 studies evaluated provided a well-defined question in an answerable form, four provided evidence of effectiveness, five applied discounting, and eight conducted sensitivity analysis. Few studies described the source used in the valuation of costs and consequences. The Drummond assessments for each of the trials evaluated can be found in Appendix 3.

Specifically the following methodological issues were present in the literature reviewed;

- Studies lacked an explicit statement of perspective and or utilize a limited analytical horizon;
- The majority of studies did not evaluate consequences (cost analysis) and are therefore limited in scope;
- Only one study has prospectively evaluated costs and consequences through a randomized control trial design[29];
- Only one cost-utility analysis has been conducted to date[29];
- No randomized trials have evaluated both the cost and consequences of a home-based program compared to supervised cardiac rehabilitation or standard care;
- The majority of studies have been conducted on populations consisting solely of myocardial infarction patients limiting the generalizability of the findings to other patient diagnostic groups.

2.5 Discussion

2.5.1 Study Population

The majority (65%) of the literature reviewed was limited to study samples consisting solely of acute myocardial infarction (AMI) patients. Two of the three cost-effectiveness trials conducted to date have been evaluations of AMI populations [29, 32]. This pool of patients utilized in these trials does not reflect the current composition of cardiac rehabilitation patients, which include coronary bypass graft, and to a lesser extent percutaneous cardiac intervention (PTCA, STENT, Endarctorectomy), angina, and heart failure patients. Most importantly these patient diagnosis groups may not benefit equally from cardiac rehabilitation interventions. Patient characteristics are expected to influence the relative cost-effectiveness of an intervention [13]. This calls into question the generalizability of earlier economic evaluation research on today's cardiac patient population. To date there is little high quality prospective trial data to support the cost effectiveness of cardiac rehabilitation in non-MI patient groups.

Women have also not been adequately represented in cardiac rehabilitation settings and are under-represented in the economic evaluations conducted to date. There is evidence to suggest differences in the cost-effectiveness of CR between the genders [45]. These differences may be explained by the fact that they are often older, more likely to be single, and had more coronary risk factors than men [51]. Women also tend to have lower levels of exercise tolerance and reduced Health Related quality of life scores at program entry than men [52]. When compared to males, women have also demonstrated higher drop-out rates and poorer adherence to supervised cardiac rehabilitation interventions [53-55].

2.5.2 Interventions Evaluated

Traditional cardiac rehabilitation program delivery consists of facility-based, supervised group exercise and counseling. The cost per life year gained resulting from cardiac rehabilitation has been found to range between $4,950 – $21,800USD [Ades, 1997 #12; [29, 32, 45] depending on the study population and type of intervention. The cost per quality-adjusted-life year was $9,200, both of which fall into the accepted range for good cost-effectiveness and cost-utility [29]. Several alternative forms of CR were evaluated within the literature reviewed including home-based programs [25, 30, 45-47]; return to work interventions [56, 57], program components and delivery characteristics [28, 48-50]. Only one modeling study has attempted to quantify the cost-effectiveness of home-based CR against standard care using modeling techniques [45]. No full prospective economic evaluation has evaluated two competing cardiac rehabilitation delivery models. The evidence to support the economic viability of these alternative delivery modes is limited to cost analysis [28, 48-50]. These alternative delivery modes will need to be evaluated via high quality full economic evaluations before they can be labeled cost-effective.

Promising future directions lie in the potential cost-effectiveness of newer program delivery models, which may use fewer program resources. Alternative CR delivery models include home-based programs with periodic face-to-face and/or telephonic counseling. Several trials have demonstrated equivalent benefits between supervised and home-based programs [25, 48]. A major benefit of home-based CR programs, are the reduced cost involved in the delivery of these programs. Specifically, savings in accommodation, overhead, equipment, and staff time are associated with home-based delivery. Interestingly, patient costs (e.g. travel, time, purchases) are likely to be larger for home-based programs. Home-based programs may

however appeal to groups of patients who may not have otherwise taken part in cardiac rehabilitation interventions. These programs may increase the proportion of patients taking part in formal programs by offering more flexible delivery models.

An area being investigated within the literature is the dose response model required to produce gains in patient quality of life and clinical status [48, 49, 58, 59]. This relates to both the frequency and duration required to maximize cost-effectiveness. In addition, components of cardiac rehabilitation including exercise, counseling, medical management will need to be evaluated to determine the incremental cost-effectiveness associated with these interventions.

2.5.3 Methodological Quality

The body of literature supporting the cost-effectiveness of cardiac rehabilitation services is characterized by limited methodological strength. Previously published systematic reviews of the cost-effectiveness of cardiac rehabilitation have documented the lack of evidence to support the cost-effectiveness of cardiac rehabilitation, particularly the lack of trials, and the poor quality of existing trials [13]. The heterogeneity in the perspectives, comparators, and type of analysis limits the ability of this systematic review to add to the strength of the evidence to support the cost effectiveness of cardiac rehabilitation. Only one trial has the strength to support such a conclusion and this study as noted has limited generalizability [29]. Recent publications [46-50] have not demonstrated improved practice, which is particularly troubling. This systematic review has found evidence to suggest the quality of economic evaluations has actually declined since the 1998 Oldridge review [13]. The quality of the economic research may be attributed to the lack of resources to support cardiac rehabilitation researchers, as well as, a lack of dissemination of best practices in the design of economic evaluations within the field. Additional high quality trials are required to validate the findings of this study and expand the generalizability of cardiac rehabilitation as a potentially cost-effective health care investment.

2.5.4 Limitations of this Review

Standard limitations of systematic reviews include the possibility that studies may have been missed in the identification process and the fact that unpublished studies are not included in the review [14, 60]. This systematic review was limited to literature published in the English language, which may introduce some bias to the reviews findings [14].
The validity of making comparisons between economic analyses conducted in different health care systems is unknown and may not be appropriate. We have included English language publications conducted in a variety of international health care settings. Since data has not been pooled studies can be analyzed and assessed independently.

In addition, a single reviewer was used to conduct all of the reviews of literature for the present systematic review. Standard practice calls for at least two reviewers to independently review the literature and address any discrepancies in the reviews via a consensus approach [14, 61]. The use of a single reviewer limits the overall validity of the review.
Several trials [5, 26-28, 30, 32, 50, 56, 57], included in the review were conducted before the implementation of new medical therapies. These new therapies have had large impacts on patient morbidity and mortality and include pharmaceutical therapies (e.g. thrombolysis, statins) which were introduced in the mid 1990s and newer intervention therapies (e.g Percutaneous Transluminal Coronary Angioplasty, STENT).

2.6 Conclusions and Recommendations

2.6.1 Conclusions

Following an extensive review, 17 trials were identified that were relevant to the economic evaluation of cardiac rehabilitation and secondary prevention services. Support for the cost-effectiveness and cost savings for health care systems resulting from cardiac rehabilitation has been identified within this review. The heterogeneity between study comparators, study designs, and perspectives makes pooling of study results inappropriate. The body of literature supporting the cost-effectiveness of cardiac rehabilitation services is characterized by limited methodological strength. To date only one trial has provided prospective randomized control trial evidence of the cost-effectiveness and cost-utility of supervised cardiac rehabilitation services [29]. Further trials are required to support the generalizability of these findings to the broader cardiac patient population. The literature evaluating home-based and alternative delivery models including the frequency and duration of cardiac rehabilitation is insufficient to draw conclusive recommendations regarding the cost effectiveness of these delivery models [25, 28, 30, 45-50]. Given the extent of the evidence to support cardiac rehabilitation as a clinically effective intervention in reducing morbidity and mortality, it has become more and more difficult to justify the ethical use of standard care comparators. There is likely to be a larger number of studies comparing competing cardiac rehabilitation delivery models (e.g standard care versus home-based). There is a strong theoretical basis to support the cost-effectiveness of home-based programs. As we continue to learn more about the characteristics and components that improve clinical outcomes of cardiac rehabilitation it will be important to also evaluate the immediate and downstream economic impact of these alternative programs.

2.6.2 Recommendations

The following recommendations are directed towards advancing policy and research surrounding the economic viability of cardiac rehabilitation.

- Greater dissemination of best practices in the design of economic evaluations is required within the field of cardiac rehabilitation. The quality of recently conducted economic evaluations, suggest a general lack of knowledge regarding the rigour required to produce quality findings. A publication reviewing characteristics of high quality evaluations and the presentation of a reference case that is specific to the cardiac rehabilitation setting for use as a guide in the design of economic evaluations is recommended.
- Well-designed trials evaluating the cost-effectiveness and cost-utility of supervised cardiac rehabilitation against standard are required to support the findings of Oldridge (1993) [29].
- There is a need to expand the evidence base supporting the economic viability of cardiac rehabilitation to the broader cardiac population including women and other diagnosis groups (e.g. PCI, CABG).
- Initiate well-designed trials evaluating the cost-effectiveness and cost-utility of alternative CR delivery models including home-based rehabilitation programs, telephonic interventions, and specific delivery model characteristics.
- Research is required to assist in identifying and understanding which patient segments will produce greater cost-effectiveness and cost-utility from comprehensive rehabilitation and other alternative delivery modes. This includes high-risk and low-risk patients, gender, age, and diagnosis groups.

Exhibit 1: Characteristics of Studies Identified in Systematic Review

Ref #	Author	Year	Title	Country	Analysis Type	Collection Years
[47]	Collins	2001	Cost analysis of gym base versus home based cardiac rehabilitation programs	Australia	Modeling Cost analysis	1996 –1998
[62]	Robertson	2001	Cost analysis of an intensive home follow-up program for first-time post-myocardial infarction patients and their families	Canada	Cost analysis	1999-2000
[44]	Georgiou	2001	Cost-effectiveness of long term moderate exercise training in chronic heart failure.	USA	Modeling cost-effectiveness	--
[45]	Lowensteyn	2000	The cost-effectiveness of exercise training for the primary and secondary prevention of cardiovascular disease	Canada	Modeling cost effectiveness	1996
[48]	Carlson	2000	Program participation, exercise adherence, cardiovascular outcomes, and program cost of traditional versus modified cardiac rehabilitation	USA	Cost analysis	-
[49]	Nieuwland	2000	Differential effects of high frequency versus low frequency exercise training in rehabilitation of patients with coronary artery disease	Netherlands	Cost analysis	-
[50]	Dixhoorn	1999	Effect of relaxation therapy on cardiac events after myocardial infraction a 5-year follow-up study	Netherlands	Utilization analysis	1981-1983
[32]	Ades	1997	Cost-effectiveness of cardiac rehabilitation after myocardial infarction	USA	Modeling cost effectiveness	N/A
[30]	Bondestam	1995	Effects of early rehabilitation on consumption of medical care during the first year after acute myocardial infarction in patients >65 years of age	Sweden	Utilization analysis	1993
[31]	Allison	1995	Medical and Economic costs of psychologic distress in patients with coronary artery disease	USA	Cost description	-
[5]	Oldridge	1993	Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction	Canada	Cost-effectiveness Cost-utility	1987-1991
[28]	Edwards	1993	Percutaneous transluminal coronary angioplasty rehabilitation: A cost-effective analysis	USA	Cost analysis	1986-1988
[27]	Ades	1992	Cardiac rehabilitation participation predicts lower hospitalization costs	USA	Cost analysis	1983-1987
[26]	Levin	1991	Cardiac Rehabilitation – a cost analysis	Sweden	Cost analysis	1991
[56]	Pilote	1992	Return to work after uncomplicated myocardial infarction: a trial of practice guidelines in the community	USA	Cost analysis	1987-1989
[57]	Picard	1989	Cost-benefit analysis of early return to work after uncomplicated acute myocardial infarction	USA	Cost analysis	1983-1985
[25]	DeBusk	1985	Medically directed at home cardiac rehabilitation soon after complicated acute myocardial infarction: a new model for patient care.	USA	Cost-minimization	1979-1983

Exhibit 2: Study Design of Studies Identified within Systematic Review

Ref	Study Aim	Perspective	Study Design	Patient Population	Sample Size	Intervention
Collins [47]	To conduct a cost analysis of a gym-based program compared to a home-based program for delivering cardiac rehabilitation services.	Program funders & patients	Modeling study	CR Referrals	Modeling based on; Gym CR; N = 95 Home CR; N = 208	Gym-based: Eight-weeks of supervised exercise (4 sessions/week) & group education Home Based: 12-month counseling intervention based on MULTFIT model
Robertson [46]	To evaluate the cost-effectiveness of a home follow-up program in reducing the rate of re-hospitalization	Health care system (in-patient / program delivery)	2-group RCT	First time MI patients, with no co-morbidities likely to affect rehabilitation	N = 66 Control; N = 34 Experimental; N=32	Experimental: Supportive educative home F/U delivered by nurses (1 session/ wk x4 wks x3 hrs) Control: Physician F/U x 2, public nurse F/U, CR optional
Georgiou [44]	To determine the cost-effectiveness of a 14-month long moderate exercise training in patients with heart failure	Limited Societal	RCT-based data modeled over 10-years	Stable New York Heart Association (NYHA) Class III Heart Failure Patients aged 55 to 64 years	Modeling based on; N=49 Exercise Therapy N= 50	Exercise Therapy was delivered in 2 phases, in phase I the patients exercise 3x/week for 8-weeks at 60% of VO2, phase II is a12-month maintenance program with twice weekly exercise.
Lowensteyn [45]	To use the cardiovascular disease life expectancy model to estimate the cost of a supervised and a unsupervised exercise program	Not explicitly stated, but appears to be societal	Modeling CEA using Cardiovascular Disease Life Expectancy Model	1992 Canadian Heart Health Survey participants (2-cohorts CVD and non-CVD)	CVD; N=1486, Non-CVD; N=7018	Supervised: group-based supervised exercise class Unsupervised: walking program performed outdoors or in a local shopping mall.
Carlson [48]	To compare the effectiveness, adherence rates, and program delivery costs of a modified versus a traditional protocol of cardiac rehabilitation	Rehabilitation program, insurer, patient	2-group RCT	First time, low to moderate risk CR patients, living less than 30 miles away, 35-75 yrs	N=80 Traditional protocol; N= 42 Modified protocol; N= 38	6-month intervention: MP = 3 exercise sessions for 4 weeks then weaned offsite + F/U by telephone + group meetings + education TP= 3 exercise sessions/wk + education
Nieuwland [49]	To determine the influence of frequency of exercise training during cardiac rehabilitation on VO2, AT, QoL and compare global costs.	Not explicitly stated, but uses the perspective of the rehabilitation program	2-group RCT	Patients with coronary artery disease	N=130	Six week intervention: High Frequency:10 sessions/wk Low Frequency: 2 sessions /wk
Dixhoorn [50]	To study the effects of breathing and relaxation therapy upon rates of cardiac events and cost-effectiveness in past MI patients	Health care system (cardiac only)	2-group RCT	Patients with a diagnosis of recent MI (within 1 month)	N=156 Exercise + relaxation; N=76 Exercise training only; N=80	Exercise + relaxation: 5-week exercise program (1-session/day) + individual instruction for relaxation (1 hour/week for 6-weeks) Exercise only: 5-week exercise program (1-session/day)
Ades [32]	To calculate the cost effectiveness of cardiac rehabilitation in dollars per year of life saved by combining published results of RCTs and documented hospital charges as compared to standard care.	Payee of health care expenses (USA = patient or insurer)	Modeling from published data	Acute MI patients	N/A	12 –week rehabilitation program versus Standard care

Ref	Study Aim	Perspective	Study Design	Patient Population	Sample Size	Intervention
Bondestam [30]	To describe the effects of the program on morbidity and utilization of medical resources outside the program during the first year after infarction.	Health care provider	Non-randomized matched study between two health care districts	Acute MI patients greater than 65 years of age.	CR; N=91 Control; N =99 71 pairs same sex and age	Home visit at 1 & 7-days post-discharge, GP visit at 1& 3-months, 6-week appt. with nurse at health centre, invitation to join a low intensity (3-5 METS) exercise group plus group discussion (1 session/wk) for 4 -8 weeks. Note: 21/ 91 patients joined the exercise group.
Allison [31]	To determine the effect of psychological distress measured with commonly used screening questionnaires, on 6-month morbidity and re-hospitalization costs in coronary patients.	Health care system (cardiac-limited)	Cohort study design (distressed and non-distressed CR patients)	Patients referred to CR following MI, CABG, PTCA, or unstable angina.	N=381 consecutive patients Distressed; N=41 (Symptom Checklist 90) Non-distressed; N=340	CR intervention included monitored exercise 1-3 sessions/week for 6 to 12 weeks plus education, pharmalogical lipid management as needed; follow-up at 3, 6, 9 months.
Oldridge [29]	To calculate the cost-effectiveness and cost-utility of an 8-week cardiac rehabilitation program in AMI patients with mild to moderate anxiety or depression as compared to usual care.	Not explicitly stated, appears to be Societal	2-group RCT (Patients stratified by work type and employment status)	Mildly to moderately anxious or depressed acute MI patients (as assessed in hospital by the Beck inventory)	Intervention; N=99 Usual Care; N=102	8-week intervention: supervised exercise with low level exercise prescription, behavioural and risk factor management counseling focused on coping strategies, individual counseling as necessary
Edwards [28]	To examine the cost-effectiveness of a cardiac rehabilitation program including exercise plus counseling versus counseling alone during PTCA rehabilitation.	Health care system	Retrospective analysis of computerized patient charge data	Patients having undergone successful PTCA intervention of an acute MI, no contraindications to exercise and insurance coverage	N=47 Exercise + counseling; N=28 Counseling only; N=19	Exercise with counseling:12-weeks of exercise (3-5 supervised sessions/wk, or home-based walking program) plus risk factor management counseling Counseling only: risk factor modification counseling
Ades [27]	To determine the effect of cardiac rehabilitation on medical costs.	Health care system (limited to hospital costs)	Non-randomized design (analysis of covariance)	MI and CABG patients	N=580 CR; N=230 Usual care; N=350	4-month intervention: 4-hours/week of exercise and risk factor teaching
Levin [26]	To compare the economic evaluation of a comprehensive cardiac rehabilitation program with standard care after MI	Societal	2-group non-randomized design (adjacent hospitals)	MI patients greater than 65 years of age	N = 305 Intervention; N=147 Control; N=158	Follow-up at a post MI clinical, education, and invitation to participate in a 3-month supervised group exercise program (2/wk) beginning 6-weeks after MI.
Pilote [56]	To evaluate the effectiveness of practice guidelines for return to work after AMI when disseminated from a University setting to a practice-based setting.	Not stated (appears to be a limited societal)	2-group RCT	Male uncomplicated acute MI patients	N=187 Intervention; N=92 Usual Care; N=92	Intervention: Treadmill test with counseling based discussion of test results
Picard [57]	To evaluate the economic consequences of an occupational work evaluation designed to identify low risk patients recovering from uncomplicated AMI and hasten their return to work.	Stated as patient (health care payee in USA)	2-group RCT	Clinically low risk male acute MI patients	N=201 Intervention; N=99 Usual Care; N=101	Intervention: Occupational Work Evaluation consisting of treadmill test and counseling session consisting of an explicit statement of risk for recurrent infarction or cardiac death and a recommendation for the time of return to work
DeBusk [25]	To compare medically directed at home rehabilitation with group rehabilitation which began 3 weeks after clinically uncomplicated acute myocardial infarction.	Not stated but is that of the Rehabilitation Program	2-group RCT	Male uncomplicated acute MI patients	N=127 Home Training; N=66 Control; N=61	MULTIFIT Intervention including 1 to 3 counseling session, in person and follow-up by telephone

Exhibit 3: Outcomes of Studies Identified within Systematic Review

Ref	Follow-up Period	Primary Outcome Measure	Outcome Collection Source	Currency / Discounting	Study Results	Sensitivity Analysis	Conclusions
Collins[47]	18-month modeling of effects	Average cost / patient Program delivery costs Re-hospitalization costs	Program Costs: Personnel, Equipment, Rent, overhead, Exercise tests, administration, materials, emergency pharmaceuticals, computer system HC Use (extrapolated from Australian data base): Hospital readmissions Patient Costs: Travel costs, opportunity cost of time, travel time	Australian Dollar 27% discount rate on equipment	Incremental cost savings of home-based program $405 Gym Based: $1,933 / person $183,597 / 95 persons Home Based: $1,169 / person $243,157 / 208 persons	7 variables: Establishment costs, years of effective life, traveling costs, patient time, leisure time value, readmission values	Home-based program more cost-effective alternative due to its ability to treat larger number of patients. May also assist in expanding reach.
Robertson[46]	6-weeks post-discharge, 6-month data collected but not reported	Health Care Costs	Program costs experimental (estimated): Nursing staff time, travel, phone, materials Health care use (review of patient records): In-patient re-hospitalization Note: emergency visits not included	Currency not reported likely CDN	Incremental Cost savings $17,216 Control: Re-hospitalization $39,200 Experimental: Re-hospitalization $12,000, Program delivery $9984.00	None reported	50% reduction in re-hospitalization achieved with home program. Intensive home F/U provided a cost-effective alternative to traditional cardiac rehabilitation programs
Georgiou[44]	14-month data modeled to 10-year horizon	$ / Life Year Saved (LYS)	Costs: equipment, space, salaries, cardiopulmonary exercise tests Wages lost due to program participation Hospitalization estimated to cost of average patient with heart failure Survival modeled from RCT [63]	USD (1999)	$1,773/LYS Cost of Program $2,054/patient Wages Lost $2,059/patient Cost hospitalization $1,336/patient Increase in Life Expectancy 1.82 years	Variables: Survival probabilities during RCT; reduction in hospitalizations; improvement provided by angiotensin converting enzymes	Long-term exercise therapy in patients with stable chronic heart failure is cost-effective and prolongs survival by an additional 1.82 years at a low cost of $1,773 per life year saved.
Lowensteyn [45]	18-year modeling	$ / Life years saved (YLS)	YLS: Modeled to life expectancy curves from 1992 Canadian Heart Health Survey data set Effectiveness: published data Program Delivery Costs (estimated): stress test, physician visits, staff time, clothing, footwear	USD (1996) Discount rate 3%	Supervised; <$15,000 / YLS Unsupervised; <$12,000 / YLS Supervised Costs; $605 (year 1), $367 (>1 year) Unsupervised Costs; $311(year 1), $73 (>1 year)	Variables; 100% and 20% adherence rates, 5% discount rate, double and half annual cost of supervised exercise program	Unsupervised exercise program is a cost-effective option. The more expensive supervised program is cost-effective for most individuals with CVD.
Carlson [48]	6-month F/U	Program delivery costs (limited)	Costs: Professional staff time, ECG testing, stress testing, blood lipids (no other program delivery costs)	USD (XXXX)	Incremental savings of MP $738 MP = $1,519.00 (30%<staff time) TP = $2,349.00	None reported	The modified protocol provided a cost saving of approximately 50%.
Nieuwland [49]	6-weeks	Program delivery costs	Staff time by vocation	Euro (XXXX)	Incremental savings $2,182 Euro High-frequency: $4,455 Euro Low-frequency: $2,273 Euro	None reported	The low frequency protocol was 5-times less costly for the exercise portion of the program.
Dixhoorn [50]	2 and 5-years	CVD event rates Cardiac re-hospitalizations rates	Search of medical records (date, duration, and diagnosis of re-hospitalizations were noted), patients mailed questionnaire, contacted general practitioner for missing data	N/A	Readmission frequency reduced 31%, Days in hospital reduced 30% after relaxation therapy Experimental: Mean # readmissions 0.68 (SD 1.07), Mean days hospitalized 6.26 (SD 11.1) Control: Mean # readmissions 0.98 (SD 1.43), Mean days hospitalized 9.0 (SD 15.9)	None reported	In the long-term, the disease course after MI is influenced favourably by giving relaxation therapy in addition to cardiac rehabilitation.

Ref	Follow-up Period	Primary Outcome Measure	Outcome Collection Source	Currency / Discounting	Study Results	Sensitivity Analysis	Conclusions
Ades [32]	15-year modeling	$ / YLS	Years of Life saved: Published data (0.202 years over 15-year period) Program delivery costs: average costs 1987-88 period as assessed by survey Health care costs: Hospitalizations, physician and non-physician services, drugs, diagnostic tests (Published Data, Ades 1992)	USD (1995) Discount rate 5%	$4950 $/YLS (1995) $2130 $/YLS (1988) Average cost of CR =$1485 (1988) Hospitalizations averted = $850 (1988)	3 variables: survival, efficacy, averted hospital expenses	Cardiac rehabilitation in the post-MI patient is more cost effective than thrombolytic therapy, CABG, and cholesterol lowering drugs though less cost-effective than smoking cessation.
Bondestam [30]	3 and 12-months after the infarction.	CVD re-hospitalization rates	Re-hospitalizations, and emergency visits, assessed by self-administered mailed questionnaire. Medical charts reviewed for additional information about hospital stay, and diagnosis. Deaths assessed from records at national registry of deaths.	N/A	CR Group: Re-hospitalizations (3mos) = 13% Re-hospitalizations (12mos) = 32% Number emergency visits = 16 Mean re-hospitalization days= 2.1 Control Group: Re-hospitalizations (3mos) = 29% Re-hospitalizations (12mos) = 47% Number emergency visits = 55 Mean re-hospitalization days = 5.4	None reported	Uncomplicated rehabilitation model characterized by very early intervention and performed within the primary health care system can significantly reduce the consumption of health care 1 year after myocardial infarction in patients ≥65 years old.
Allison [31]	6-months post hospitalization	Costs associated with CVD re-hospitalizations	Re-hospitalizations determined by review of Mayo Clinic medical records, personal interviews with patients during routine follow-up, mail survey with patients missing follow-up and by telephone with non-responders to survey.	USD (XXXX)	Mean re-hospitalization Costs: Distressed = $9,504 Non-distressed = $2,146 Incremental costs = $7,358 Mean re-hospitalizations: Distressed = 2.3 +/- 1.0 versus 1.2 +/- 0.5 ($p<0.000$) in non-distressed	None reported	These data add support to the hypothesis that psychological distress adversely affects the prognosis of coronary patients.
Oldridge [29]	4, 8, 12-months from hospital discharge	$ / QALY $ / YLS	Survival data:(published meta analysis): (LYG 0.022 year/patient in favour rehab) Utility: TTO Program Costs (measured): Rent, Equipment (10 y), Staff salaries, printed resources Patient costs (collected by survey): Health services use (collected by survey): Reported number of visits physicians, hospital emergency, allied health, medications	USD (1991) Discount rate of 5% for equipment	$9,200 / QALY over 1-year (min $4,400, max $24,600) $6,800 over 3-years (min $3,200, max $18,000) $21,800/ LYG (min $10,500, max $58,200) Incremental savings $480/ patient (min. $230 and max $1,280) Costs: $790 / patient Cost Savings: $310 for intervention	Differences in the lower and upper limits of the mean time trade off scores, Cost effectiveness Discounted at 0 and 10%, min, mean, max costs	The data provide evidence that brief CR initiated soon after AMI for patients with mild to moderate anxiety or depression, or both, is an efficient use of health-care resources and may be economically justified.

Ref	Follow-up Period	Primary Outcome Measure	Outcome Collection Source	Currency / Discounting	Study Results	Sensitivity Analysis	Conclusions
Edwards [28]	12-months post PTCA	Total costs (CR delivery costs + CVD health care expenditures)	Patient hospital and cardiology records searched for services and expenses for discharge medication regimens the cardiology clinic (fees, ECG, GXT, holter monitoring, x-rays, biochemical analyses) cardiac related hospital readmissions, and cardiac related hospital outpatient visits, CR phase II and II expenses.	USD (XXXX)	Cost savings of $2597 in exercise + counseling group. No significant differences between groups. Exercise + Counseling: $1686 Counseling only $4283	None reported	The adoption and maintenance of a lifestyle modification program with exercise training after PTCA (supervised or unsupervised) appears to be economically beneficial.
Ades [27]	Began 3 months after cardiac event and continued 1 to 46 months (mean 21 months)	Per capita hospitalization charges	Hospitalization charges: Computerized review of billing data used to determine admission diagnosis, clinical events, days of hospitalizations Note: out of state hospitalizations not included, physician charges not included	USD (1992)	Per capita hospitalization charges $739 lower in CR group Hospitalization charges per capita; CR = $1197 +/- 3911 USC= $1936 +/-5359	None reported	Results of this study show an association between participation in comprehensive CR and lowered cardiac re-hospitalization costs in the years after an acute coronary event.
Levin [26]	5-years	Incremental patient costs, Program delivery costs, Health care costs in dollars	Program costs; salaries, administrative overheads, facilities, equipment, patient travel costs Health care: re-hospitalizations (days), outpatient visits Patient: Sick leave days, time costs of visits	Swedish Krona (XXXX) Discount rate 5%	Incremental Costs over 5-year period = SEK 73,510 Training program = SEK 1530 (1988) Mean readmission for CVD disease; I= 1.6 (SEK 22,480), C= 2.2 (SEK 31,050) Total costs (direct + indirect); I= SEK 484,260, C= SEK 557,770	Sensitivity analysis with Discount rate varied between 0-10%. Did not change conclusions	The comprehensive CR program is a major strategy that leads to both lowered costs and positive health effects. The CR program is therefore highly cost effective.
Pilote [56]	1, 3, and 6-months after MI	Mean days for return to work	Questionnaire, chart review, and telephone interview documented the timing of return to work and rates of cardiac death, angioplasty, CABG, recurrent MI.	N/A	Mean days for return to work I = 54 days, UC = 67 days, (p=0.2) Patients without ischemia (p=0.008) I= 38, UC = 65	None reported	Practice guidelines developed were not as successful in hastening return to work after AMI when tested in a practice setting.
Picard [57]	6-months	Per capita benefit (dollars)	Telephone interview and questionnaire utilized for: Re-hospitalization, diagnostic tests, cardiac procedures, return to work (days), occupational income, Program delivery costs (treadmill test, staff time for counseling)	USD (XXX) No discounting	Per capita benefit $6,685 intervention vs. $4,081 Usual Care Means Return to Work (p<0.002) I = 51 days, UC = 75 days Medical costs: I= $2,970, UC= $3,472 Income: I= $9,655, UC=$7,553	Range of charges from 3 hospitals taking part in investigation.	Projected to the >300,000 low risk, employed survivors of AMI annually, the savings generated by the occupational work evaluation could yield an annual economic benefit of >800 million.
DeBusk[25]	2-years	Program delivery costs	Equipment, professional staff time, administration	USD (XXXX) No discounting	Supervised: $720 / patient Home: $328 / patient	None reported	Medically directed at home rehabilitation has the potential to increase the availability and to decrease the cost of rehabilitating low-risk survivors of AMI.

Exhibit 4: Summary of Drummond Evaluations

Drummond Criteria	Collins	Robertson	Georgiou	Lowenstyn	Carlson	Nieuwland	DixHoorn	Ades	Bondestam	Allison	Oldridge	Edwards	Ades	Levin	Pilote	Picard	DeBusk
1. Was a well-defined question posed in an answerable form?	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N
2. Was a comprehensive description of competing alternatives given?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
3. Was there evidence that the programmes' effectiveness had been established?	N	N	Y	N	N	N	N	Y	N	N	CT	N	Y	Y	N	Y	N
4. Where all the important and relevant costs and consequences for each alternative identified?	Y	Y	Y	Y	Y	N	N	N	N	N	Y	N	N	Y	N	Y	N
5. Were costs and consequences measured accurately in appropriate physical units?	Y	N	N	N	N	CT	N	Y	N	N	Y	CT	Y	Y	Y	Y	N
6. Were costs and consequences valued credibly?	N	N	Y	N	N	N	N	CT	N	N	CT	CT	CT	CT	N	Y	CT
7. Were the costs and consequences adjusted for differential timing?	N	NA	Y	Y	Y	N	N	Y	N	Y	N	N	N	Y	N	N	N
8. Was an incremental analysis of costs and consequences of alternatives performed?	Y	Y	Y	Y	Y	N	N	Y	N	N	Y	N	Y	Y	N	N	N
9. Was a sensitivity analysis performed?	Y	N	Y	Y	Y	N	N	Y	N	N	Y	N	Y	Y	N	Y	N
10. Did the presentation and discussion of study results includes all issues of concern to users?	Y	N	N	Y	N	N	N	Y	N	N	Y	Y	Y	Y	Y	Y	N

Master of Health Administration
School of Management
University of Ottawa

CHAPTER 3:

Economic Evaluation of Standard versus Distributed Cardiac Rehabilitation Program Delivery

Executive Summary

BACKGROUND: The growing number of aging Canadians and continuing constraints on health care resources accentuates the need to develop and disseminate cost-effective interventions for the prevention and management of cardiovascular disease. Exercise-based cardiac rehabilitation programs (CRPs) have been recognized as cost-effective interventions resulting in decreases in all-cause mortality, improvements in patient quality of life, and cardiac risk factors compared to standard care. Little is known about the relative cost-effectiveness of different cardiac rehabilitation program designs and how cost-effectiveness may be influenced by patient characteristics. The evaluation of alternative CRP delivery models will add to our understanding of how best to design and fund cardiac rehabilitation services to maximize outcomes for patients and the health care system.

OBJECTIVES: To compare two alternative forms of cardiac rehabilitation program delivery, an intensive (3-month, 33-session) versus a distributed (12-month, 33-session), for indices of cost-utility from the perspective of the health care system, using data from a 2-year randomized clinical trial conducted at the University of Ottawa Heart Institute.

DESIGN: The present economic analysis was conducted alongside a two group randomized control trial with groups balanced on gender and random assignment to either an intensive (3-month, 33-session) or a distributed (12-month, 33-session) program of cardiac rehabilitation. The intensive group was scheduled for supervised exercise twice weekly over three months while the distributed program exercised weekly for 3 months, then bi-monthly for 3-months, and monthly for the last 6-months. Patients were assessed at baseline, 3, 6, 12, 15, and 24-months.

POPULATION: A total of 396 patients with Coronary Artery Disease, referred to cardiac rehabilitation, willing to provide informed consent, proficient in English and geographically available for intervention and follow-up were randomized to one of the two intervention arms.

MAIN OUTCOME MEASURES: Outcome measures evaluated include incremental; program delivery costs, health care use limited to cardiac related events, Quality Adjusted Life Years (QALYs) gained as measured by the time trade-off tool.

RESULTS: The 3-month intervention was found to be dominant ($16,228/QALY), resulting in both a savings to the health care system and larger gains in QALYs over the 2-years following initiation of CRP. Stratified analyses suggest the standard 3-month program was a more cost-effective intervention for higher risk and CABG patients. The 12-month program was more cost-effective for lower risk patients and females.

CONCLUSION: A shorter more intensive intervention was found to be dominant as compared to a 12-month CRP. Important differences were noted in the cost-effectiveness of CRP across cardiac risk strata and diagnosis groups, suggesting patients may benefit form triage to available CRP models.

RELEVANCE: This study is the first full economic evaluation to evaluate alternative program delivery of cardiac rehabilitation services. This is also the first cost-utility analysis to utilize a broad based cardiac rehabilitation patient population. The study's findings will make a significant contribution to our knowledge about how best to design cost-effective cardiac rehabilitation interventions.

3.1 BACKGROUND

3.1.1 Cost-Utility Analysis

Cost-effectiveness analyses (CEA) are an important tool for the evaluation of competing health care interventions. The aim of the CEA is to compare the cost and effects of one treatment against one or more alternatives treatments [64]. CEAs move beyond mere assessment of financial expenditures to include an assessment of effectiveness of health outcomes of interest. The C/E ratio forms the basis of all cost-effectiveness analysis, where net health care expenditures form the numerator and net improvement in health forms the denominator (Cost/Effect). Data can be analyzed from a variety of perspectives (societal, health care system, patient). The perspective that is selected will direct the inclusion or exclusion of specific data in the numerator [65]. When health outcome include quality of life, the analysis is termed "cost-utility analysis" (CUA) [12]. CUA is generally seen as a special case of CEA [40]. CEAs can assist with more effectively allocating limited health care resources and informing policy.

Incremental cost-utility analyses (ICUA) are CUAs in which the differential costs and effects of program delivery are considered. ICUAs are the preferred method for comparing two treatments. A high incremental cost-effectiveness ratio implies that a large expenditure will be required to achieve the extra benefit and is less economically attractive than a low incremental cost effectiveness ratio. The incremental cost-utility ratio is calculated as;

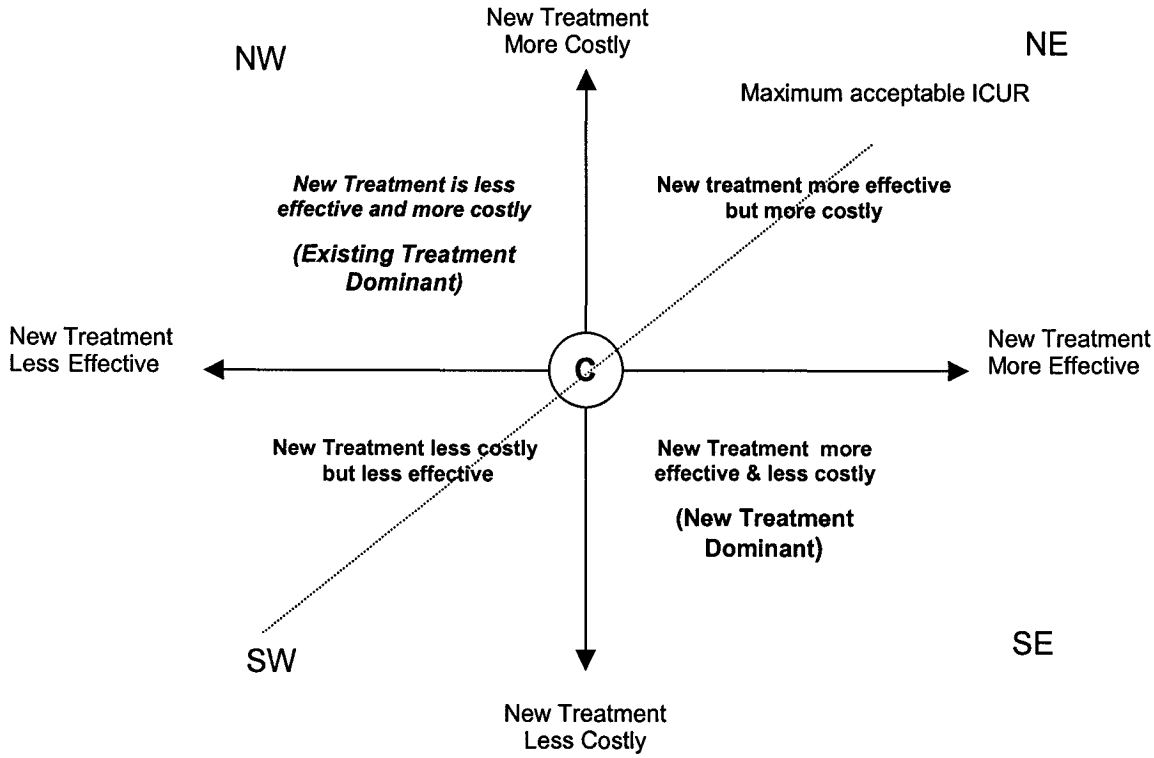
$$\frac{\text{(Mean Program cost of experimental treatment – Mean Program cost of existing treatment)}}{\text{(Mean QALY gain for experimental treatment – Mean QALY gain for existing treatment).}}$$

Four possible situations can arise when comparing ICU between two treatments (experimental and existing) [54]:

1) The experimental therapy is less expensive and more effective than existing therapy (Experimental therapy is deemed to be "Dominant")
2) The experimental therapy is more expensive and less effective than existing therapy (Existing therapy is deemed to be "Dominant")
3) The experimental therapy is more expensive and also more effective than existing therapy
4) The experimental therapy is less expensive and less effective than existing therapy

These four possibilities are illustrated in the four quadrants of the cost-effectiveness plane presented in Figure 3.1. The horizontal and vertical axes represent the incremental effects and costs, respectively. Cost-effectiveness ratios of greater than zero (>0) occur when the experimental health care intervention has both higher costs and greater effectiveness than existing therapy. Ratios of less than zero (<0) occur when the existing intervention "dominates" over the experimental therapy by resulting in lower costs and greater effectiveness than the comparator [66]. The north east (NE) and south west (SW) quadrants of the cost-effectiveness plane represent interventions, which present a trade-off between greater benefits (situation 3) or greater savings (situation 4). The value of the trade-off between benefits and costs is assessed by evaluating the treatment against the maximum acceptable incremental cost utility ratio (ICUR) represented in Figure 3.1 by a diagonal axes. Treatments which fall to the right of the maximum acceptable ICUR are considered economically attractive.

Figure 3.1: The cost-effectiveness plane
Source: Modified from Drummond 2001



3.1.2 Economic Evaluation of Cardiac Rehabilitation

A Systematic review of the economic literature surrounding cardiac rehabilitation and secondary prevention services was conducted (See Chapter 1 for detailed report). Support for the cost-effectiveness and cost savings to the health care system of CR was identified within the systematic review. The body of literature supporting the cost-effectiveness of CR services is weak, characterized by a lack of trials, and the poor quality of existing trials [13]. To date only one trial has provided a prospective randomized control trial evidence of the cost-effectiveness and cost-utility of supervised CR services [29]. Additional high quality trials are required to validate the findings of this study and expand the generalizability of CR as a potentially cost-effective health care investment.

3.1.3 Innovative Cardiac Rehabilitation Program Delivery

A number of innovative program delivery models are being developed for the delivery of cardiac rehabilitation services. These alternative program delivery models attempt to utilize fewer resources to deliver equivalent outcomes, or maximize outcomes delivered through services of equivalent cost.

The optimal frequency and duration of cardiac rehabilitation programs, to produce important gains in patient quality of life and clinical status, as well as, maximize cost effectiveness is unknown. The benefits derived from CR are directly dependant on the long-term adherence to physical activity and other lifestyle changes adopted during the intervention period. The limited ability of short-term CR interventions to develop long-term patient behaviour change has called into question the cost-effectiveness of cardiac rehabilitation services. There is evidence that between one quarter and one half of CR participants are exercising one year following the initiation of CR [67-69]. Well-designed interventions that promote long-term maintenance of important lifestyle changes are needed.

Nine published studies have conducted cost-analysis of alternative delivery models of which, five have evaluated home-based CR programs [25, 30, 45-47], and 4 have evaluated alternative supervised CRP delivery models [28, 48-50]. Two studies have assessed the impact of frequency and or intensity of CR delivery [48, 49]. Nieuwland (2000) compared the global costs and clinical effectiveness of a high frequency (10-sessions per week) and low frequency (2-sessions per week) CR program [49]. The low frequency protocol as expected was 5-times less costly [49]. Carlson (2000), compared the adherence rates and program delivery costs of a modified vs. traditional protocol of CR [48]. The traditional protocol consisted of 3-weekly exercise sessions over three months plus education. The modified protocol began with 3 exercise sessions per week for four weeks and then weaned patients to off-site exercise over a 12-month intervention period supported by telephone follow-up and group meetings. The modified protocol was found to provide a cost savings for the rehabilitation program of approximately 50% compared to the traditional protocol. The authors did not evaluate health care use of participants or include a measure of cost-effectiveness. The methodological quality of economic evaluation comparing innovative delivery models is limited to cost analyses and questions remain concerning the relative CE of different program designs [28, 48-50]. These and other innovative alternative delivery modes will need to be evaluated via high quality full economic evaluations before they can be labeled cost-effective.

3.1.4 Study Rationale

To date, optimal program duration and frequency for cardiac rehabilitation has not been identified. The length of CR services in Canada is highly variable ranging from 2-months to 2-years and is limited by third party reimbursement to 12-weeks in the U.S [24]. Frequency of CR has also varied from 1 to 5 supervised sessions per week. The standard for CR program delivery has consisted of supervised facility-based exercise sessions 2-3 times per week over a 3-month period (36-sessions) [24]. Participation in a standard 12-week CR program is known to result in positive changes in exercise tolerance, blood lipids, and quality of life in patients with CAD [58]. There is evidence that patients gain additional benefit from extending program length over longer periods [58]. Behaviour change lifestyle theories suggest that patients may require more time than is currently available in standard length CRPs to establish new lifestyle patterns (e.g. smoking cessation, healthy eating, regular physical activity) [70, 71]. Authors have acknowledged the importance of extending CR program length beyond the standard 12-weeks and developing maintenance programs to ensure long-term behaviour change [58, 67]. The potential cost effectiveness of innovative program delivery models, which may use fewer program resources or maximize the benefits gained from program delivery investments, has intrigued clinicians and researchers in recent years. Evaluating these alternative program delivery models will add to our understanding of how best to design CR models to maximize outcomes for patients and the health care system.

The present study will compare two alternative forms of CR program delivery, a standard (3-month, 33-session) versus a distributed (12-month, 33-session), for indices of cost-effectiveness and cost-utility from the perspective of the health care system, using data from a 2-year randomized clinical trial conducted at the University of Ottawa Heart Institute. Traditionally the extension of intervention duration has been associated with increased program delivery costs. By keeping the total number of program contacts equal and distributing the sessions over longer periods of time, program efficacy and overall cost-effectiveness of CR program may be improved. The study utilizes best practices in research design and will make a significant contribution to our knowledge about how best to design cost-effective CR interventions.

3.2 Objectives

3.2.1 Objective

To compare, in patients with Coronary Artery Disease (CAD), a standard 3-month (33-session) versus a distributed 12-month (33-session) program of cardiac rehabilitation as measured one and two years following program intake for indices of incremental cost utility evaluated from the perspective of the health care system (cardiac). As a secondary objective the relative cost-effectiveness of program delivery models across cardiac patient clinical and demographic groups.

3.2.2 Hypothesis

i. **Cost Determination**

a. Two years following program intake no significant differences in program delivery costs will be found between a 3-month (33-session) and 12-month (33-session) program of cardiac rehabilitation.

b. Two years following program intake a cost savings in health care use will be found in the12-month cardiac rehabilitation program.

ii. **Incremental Cost Utility**

a. Two years following program intake, the 12-month cardiac rehabilitation program will be result in lower cost per quality adjusted life year (QALY).

b. Stratified analysis will identify differences in the cost-effectiveness between the 3-month and 12-month programs of cardiac rehabilitation amongst patient groups.

3.3 Methods

3.3.1 TYPE OF ANALYSIS

An incremental cost-utility analysis was conducted to measure outcomes in terms of quality-adjusted life years (QALYs) gained. Differences in direct costs were also evaluated.

3.3.2 TARGET AUDIENCE

The primary target audience is the decision maker for funding secondary prevention programs (Ministry of Health and Long Term Care), as well as, the cardiac rehabilitation program who may be selecting between various delivery models.

3.3.3 PERSPECTIVE

Costs were evaluated from the perspective of the health care system and will focus solely on costs related to Coronary Artery Disease. The choice to include only those costs related to CAD reflects the expected incremental impact of the intervention.

3.3.4 SETTING AND POPULATION

This study was conducted between September 1999 and April 2003 at the University of Ottawa Heart Institute Prevention and Rehabilitation Centre (UOHIPRC). A total of 396 patients with CAD, referred to the UOHIPRC, willing to provide informed consent, proficient in English and geographically available for intervention and follow-up were randomized to one of the two intervention arms. Patients were stratified according to gender. Documentation of CAD was based on: (1) a documented myocardial infarction (MI); (2) a clinical history typical of angina pectoris together with a treadmill test result or nuclear scan consistent with myocardial ischemia; (3) previous coronary bypass graft (CABG), or percutaneous coronary intervention (PCI). Exclusion criteria included: referral following cardiac transplantation; implantation of automatic defibrillator; or contraindications to exercise.

Sample size was calculated based upon 80% power for detecting clinically meaningful differences in measures of effectiveness. Health related quality of life was the parameter requiring the largest sample size (N=315) to detect differences between groups. Twenty percent was added to the sample size to allow for attrition in the sample over the two-year follow-up period.

3.3.5 STUDY DESIGN AND TREATMENT COMPARATORS

The present economic analysis was conducted alongside a two group randomized control trial with groups balanced on gender and random assignment to either standard CR (3-month, 33-session) or distributed CR (12-month, 33-session) program.

Both intervention groups received the same number of CR program contacts (total of 33), however, the schedule of contacts varied by intervention group assignment (see Table 1). Four types of contacts were provided, including: 3-case manager contacts, 1-medical management visit, 2-educational workshops, and 27-supervised exercise class visits (see Table 3-1). Case manager contacts consisted of two face-to-face visits and one telephone contact. The first visit was used to assess the patient's goals and needs and triage participants into optional program components (e.g. stress management, nutritional counseling). At the later case manager visits, progress was reviewed. The physician visit was a single face-to-face meeting with a program physician to ensure adequate risk factor control. Both intervention groups received the same number of supervised exercise sessions (total of 27), however, the schedule of contacts varied by intervention group assignment (see Table 3.1). Patients in both intervention arms were encouraged to exercise outside the scheduled supervised exercise sessions for a total of 100-200 minutes per week or 1500kcals.

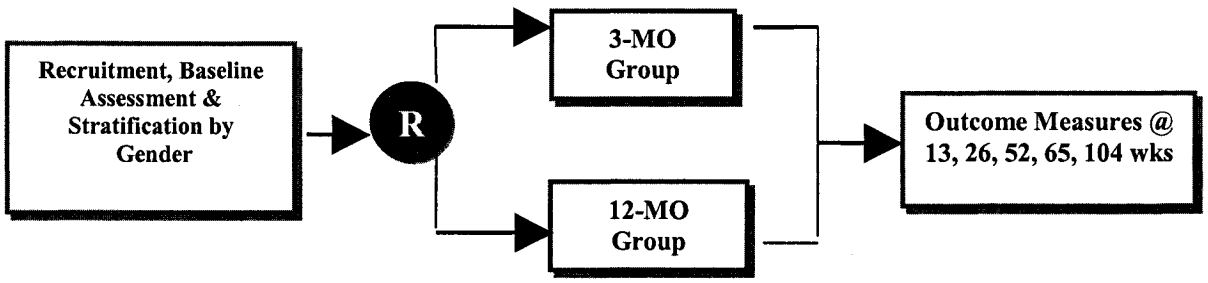
Table 3.1: Schedule of program contacts in the three-month and twelve-month program groups

Type of program contact	Standard CR (3 MO)	Distributed CR (12 MO)
Case manager office visits	Week 1, 4, 8	Week 1, 8, 26
Medical management visits	Week 7	Week 7
Education workshops	Week –2, -1	Week -2, -1
Exercise classes	Week 1 - 13 (2x / week), Week 14 (1x / week).	Week 1 –14 (1x / week), Week 16 – 28 (1x / 2weeks), Week 32-52 (1x / month)

3.3.6 ANALYTICAL HORIZON

The primary analytic horizon captured 2-year study outcomes generated from the prospective experimental design. Follow-up data collection occurred 13, 26, 52, 65, and 104 weeks after program intake via questionnaire and face-to-face interviews. Figure 3.2 provides an overview of the experimental design.

Figure 3.2: Overview of Experimental Design



3.4 PRIMARY OUTCOME MEASURES FOR COST-UTILITY ANALYSIS

3.4.1 Resource Identification, Measurement, and Valuation

3.4.1.1 Identification of Resources

A detailed treatment path schemata was developed to describe the therapeutic pathway of patients involved in each of the experimental groups (Appendix 5). The schemata, serves to describe potential downstream events over the 2-year follow-up period and was used to identify relevant resource categories. Primary outcome measures include program delivery costs (staff time per patient, overhead cost, equipment, tests/procedures), health care utilization (physician visits, emergency room visits, tests, procedures), visual analog scale, time trade-off, morbidity, mortality. Costs have been broken down into two broad cost related categories; intervention delivery costs and health care services costs. Appendix 6 provides an overview of the key study variables.

3.4.1.2 Intervention Delivery Costs

The principal resource items of interest are the individual sessions within the CR program including exercise classes, medical consultations, and individual counseling sessions with a member of the CR professional staff (e.g. dietician, psychologist). The cost of sessions for the CR program was measured using a bottom up costing methodology, which involves recognition of the individual resource items (such as staff time, accommodation and overhead) comprising the composite resource.

3.4.1.3 Health Care Services Use

Health care services costs were limited to cardiac related costs, assessed from the perspective of the health care system. The use of additional health care resources was estimated by questionnaire delivered to patients at each of the follow-up time points (See Appendix 7). The questionnaire asked participants to report medical test/procedures, physician visits, and days hospitalized in the month preceding questionnaire completion. The study coordinator reviewed questionnaires with participants each follow-up evaluation to ensure the accuracy of the data. Resource consumption was measured in natural units (number of physician visits, hospitalization days, number of laboratory and diagnostic tests and procedures) and presented by category including in-patient, emergency, outpatient visits. Clinical events, including death, MI, repeat revascularization, were tracked from the date of randomization until the end of the 2-year follow-up.

3.4.1.4 Cost Valuation

Costs per patient will be calculated as the product of each patient's use of resources and the corresponding unit cost in Canadian Dollars (CDN 2002). A summary of the cost and sources used in the valuation of health services in provided in Appendix 8. Available cost data from the UOHI was used for the calculation of professional staff wages, accommodation, and overhead. The cost of medical and exercise equipment was obtained from purchase records. Equipment costs (10-year amortization) were adjusted to reflect 2002 costs using a discount rate of 5%.

Cost per weighted case for most cardiovascular procedures (CABG, PCI, STENT, endarctoectomy, pacemaker implant) was obtained from the Ontario Joint Policy and Planning Committee (JPPC) [72, 73]. The cost of in-patient hospitalizations for myocardial infarction, heart failure, angina was also obtained from the JPPC [34]. The cost of outpatient diagnostic testing (cardiopulmonary stress test, echocardiogram) was obtained from Ontario Hospital Insurance Plan (OHIP) schedule of benefits which allows estimation of the unit costs of resources based on standard methods of cost allocation. The costs of additional health care resource use, such as, emergency visits, primary care visits, additional specialist consultations, were obtained from OHIP premiums [74].

3.4.2 Quality Adjusted Life Years

Quality Adjusted Life Years (QALYs) were calculated using the area under the curve method. Quality Adjusted Life Years (QALYs) gained was the unit of analysis used within the CUA, and serves as a proxy of both quantity of life and quality of life [75]. Preference weight values are measured on a 0 (death) to 1.0 (full health) scale.

3.4.2.1 Time Trade-off

The Time Trade-off (TTO) was used to describe the health status of subjects. The technique consists of a TTO question that is prefaced with a visual analog scale ranking of current health status (See Appendix 9). The visual analog scale is a 0 to 100-point scale with anchors of death and perfect health. Patients were asked to indicate their current health state as a percentage on this scale. The TTO question asks subjects to consider an average life expectancy for a person their age and indicate how many years of life they would be willing to give up to be in perfect health. The TTO follows a ping-pong methodology in which a subject's response to a question leads to a second TTO question with new parameters. The time period of full health is varied until the respondent is indifferent between the two alternatives. The preference score is determined by a ratio between the number of years (x) a patient is willing to spend in the indifferent health state over the total number of years of life expected for his/her age (t) (i.e. x/t) [11]. The TTO has been applied in clinical studies, economic evaluations, and the measurement of population health [75-77]. The TTO was selected because it has been found to be simpler for respondents to comprehend than other direct utility measures [11].

3.4.3 DISCOUNTING

Costs were discounted to reflect values in Canadian Dollars (CDN 2002). A discount rate of 5% per year was used as the base case with the rate varied by means of sensitivity analysis to reflect a discount rate of 0% and 3% [40].

3.4.4 COST-UTILITY MODELING

Descriptive statistics were used to describe the characteristics of the two experimental groups. Baseline characteristics in experimental groups was compared using two-tailed independent-group 't' tests for continuous variables and chi-square tests for categorical variables. Between group differences in costs and utilities were assessed using two-tailed independent t-tests. The incremental cost-utility ratio was calculated as: (Program cost of 12-month treatment - Program cost of 3-month treatment) / (Mean QALY gain for 12-month treatment - Mean QALY gain for 3-month treatment). The measurement of quality adjusted life years (QALYs) was calculated for the 2-year period for which utility values are measured using the area under the curve methodology.

3.4.5 UNCERTAINTY

3.4.5.1 Confidence Intervals

Where appropriate, the differences between experimental groups was represented by 95% confidence intervals. Uncertainty due to sample size and measurement errors was accounted for using Monte Carlo simulations. The Monte Carlo simulation method allows values in which uncertainty is presumed to exist to be varied simultaneously. Confidence intervals were created for the incremental cost-effectiveness ratios based on the bootstrap technique [78]. The bootstrap is a Monte Carlo re-sampling technique where observations are randomly drawn with replacement from observed cost and QALY data to construct an empirical probability density function [64]. Bootstrap techniques provide methods for constructing CI for any distribution [79]. A computer based (Crystal Ball Software) random number generator was used to develop pseudo-data sets of paired data from the original data set. A total of 10,000 CB bootstrap samples were performed (B = 10,000). The re-sampled means were used to calculate the 2.5^{th} and 97.5^{th} percentiles.

3.4.5.2 Sensitivity Analysis

Sensitivity analyses were used to evaluate the robustness of conclusions of the cost effectiveness analysis where significant assumptions have been made. The values identified for sensitivity analysis were used to recalculate the cost-utility and cost-effectiveness ratios as appropriate using the Monte Carlo techniques described above. The following assumptions will be subject to sensitivity analysis:

1) overhead (14% actual UOHI, and 30%, the average for a health care organization);
2) emergency visits (SD of 50%);
3) cardiac tests (SD 50%);
4) cardiovascular procedure costs (reported SD).

Sensitivity analysis was conducted using upper and lower range of costs and outcomes where means have been used including;

1) physician fees (min, max);
2) psychology minutes (min, max);
3) utility weights (95% CI);
4) discount rate (0%, 3%, 5%).

3.4.6 STRATIFIED AND SUB-GROUP ANALYSIS

3.4.6.1 Stratified Analysis

Differential cost and quality adjusted life years are hypothesized amongst patient sub-groups within the cardiac population. Important differences between patient groups were explored using stratified and sub-group analyses. Information from these secondary analyses is intended to be used to develop hypothesis about the relative cost effectiveness of the 3-month and 12-month interventions amongst segments of the cardiac population [40]. Stratification variables were identified a priori to reflect important patient sub-groupings as defined by;

a) Risk Strata

The risk stratification technique developed by the Canadian Association of Cardiac Rehabilitation (CACR) and the American Association of Cardio-pulmonary Rehabilitation (AACVPR) were used to model 2 separate risk scores [23]. The CACR and AACVPR risk stratification models have been developed based on epidemiological data from the Framingham study and categorize patients into moderate, high, and very high-risk categories. The CACR risk stratification tool generates two stratification scores for acute risk and the risk of disease progression, as well as, an overall risk score[23].

b) **Cardiac Diagnosis**

Four possible referring diagnosis were eligible for study participation; coronary artery bypass graft (CABG), percutaneous coronary interventions (PCI) including angioplasty, stent implantation, and endarctorectomy, myocardial infarction (MI), and angina pectoris. Few authors have examined the cost-effectiveness of cardiac rehabilitation in non-MI patient populations. Patient diagnosis groups may not benefit equally from cardiac rehabilitation interventions. Little is known about the relative cost effectiveness of different cardiac rehabilitation program delivery models for patients recovering from various cardiac procedures or events. The rehabilitation of cardiac patients will differ based on cardiac procedure or event. PCI patients experience limited disability as compared to CABG patients who have significant rehabilitation needs.

c) **Participant Age**

Four categorical age groupings were assessed (<55, 55-64, 65-74, ≥ 75). Age categories have been arbitrarily developed to represent categories above and below 65 years of age, very young, and older patients. It is hypothesized that patients of different ages may have different cardiac rehabilitation needs and may benefit from triage to programs which can best meet these needs.

d) Gender

There is evidence to suggest differences in the cost-effectiveness of CR between the genders [45]. These differences may be explained by the fact that women are often older, more likely to be single, and had more coronary risk factors than men [51]. Women also tend to have lower levels of exercise tolerance and reduced health related quality of life scores at program entry than men [52].

3.4.6.2 Sub-group Analysis

Sub-group analysis was used to further isolate the efficacy of the interventions being compared. A two-group categorization of participants baseline TTO score as maximal (equal to 1.0) was used to distinguish between patients who are unlikely to gain further quality of life benefits from the rehabilitation intervention. A second sub-analysis involves the evaluation of data from the surviving study sample at the end of 2-years. Deceased patients due to cardiac or non-cardiac death were assigned a QALY score of 0. Finally, the incremental cost-effectiveness between intervention arms was evaluated in patients with an intervention compliance of 80% or greater.

3.5 Results

3.5.1 Sample Population

3.5.1.2 Sample Size and Loss to Follow-up

A total of 396 patients were randomized to either the 3-month (N=198) or 12-month (N=198) intervention arm with stratification based on gender. The study population represented 65.5% of eligible patients participating in cardiac rehabilitation during the study recruitment period. Two patients from each group were excluded from the sample post-randomization. The reasons for exclusion included pregnancy (1), incorrect CAD diagnosis (2), and inadequate English language comprehension (1). Exhibit 10 provides a detailed overview of data return over the 2-year follow-up period.

The two-year study dropout rate/lost to follow-up rate was 22.7%. A summary of the reasons for loss to follow-up for each intervention arm and overall is provided in Table 3.2. The most common reason for loss to follow-up was patient request to be withdrawn from the intervention and the associated follow-up. The majority of with-drawls occurred in the first 3-months following randomization.

Active study participants were defined as participants who were neither, excluded, or withdrawn from the study sample. A total of 156 active participants were in the 3-month group and 150 in the 12-month group. Exhibit 5 provides a comparison between the patient characteristics of study dropouts and active patients. A higher dropout rate was observed amongst female participants 36.1% (22/61) compared to 20.1% (68/328) amongst male participants. Significant differences were also noted in education and cardiac risk strata between active participants and dropouts. Data availability for each assessment point is summarized in Table 3.3 for active participants.

Table 3.2: Summary of reasons for loss to follow-up between intervention groups

Reason for Loss	Standard (# of patients)	Distributed (# of patients)	Overall (# of patients)	p-value
Ineligible	2	2	4	Ns
Transferred to Home program	4	2	6	Ns
With drawl pre-intervention	7	5	12	Ns
With drawl	19	26	45	Ns
Lost	3	8	11	Ns
Illness (psychiatric, disease)	7	5	12	Ns
Total In-Active	42	48	90	Ns
Total Active	156	150	306	Ns

Table 3.3: Summary of Data Availability for each follow-up assessment

Time-Point	Standard N (%*)	Distributed N (%*)	Overall N (%*)	p-value
Baseline	157 (100)	149 (100)	306 (100)	Ns
3-month	152 (96.8)	141 (89.9)	293 (95.7)	Ns
6-month	144 (91.7)	134 (94.9)	278 (90.8)	Ns
12-month	151 (96.1)	141 (94.6)	292 (95.4)	Ns
15-month	129 (82.1)	138 (92.6)	277 (90.5)	Ns
24-month	149 (94.9)	131 (87.9)	280 (91.5)	.026

* Proportion of data available for active participants

3.5.2 Patient Characteristics

The cost-utility analysis was conducted using data set of 306 active study participants. Table 3.4 provides a summary of characteristics of the active study participants. The mean age of the study sample at baseline was 58.4 years (+/-9.7), 86.8% male, with an average of 15.0 years (+/-4.0) of formal education. The referring medical diagnosis of the sample population was CABG (45%), PCI (36.8%), MI (11.4%), angina pectoris (6.8%). There were no differences in the clinical and demographic profiles of intervention groups noted at baseline (See Exhibit 11).

Table 3.4: Characteristics of Active Study Participants (N=306)

Patient Characteristic	Overall	Standard (a)	Distributed (b)	p-value
Mean Age (SD)	58.4 (9.7)	58.4 (9.5)	58.4 (10.7)	ns
Gender				
% Male	86.8	84.5	89.3	ns
% Female	13.2	15.5	10.7	
Cardiac Diagnosis*				
% CABG	45.0	43.6	46.4	ns
% PCI	36.8	39.7	33.8	
% MI	11.4	10.9	11.9	
% Angina	6.8	5.8	7.9	
Mean Years Formal Education (SD)	15.0 (4.0)	15.1 (4.1)	14.9 (4.0)	ns
Cardiac Acute Risk Strata **				
% High	20.2	18.6	21.9	ns
% Moderate	49.8	55.1	44.4	
% Low	30.0	26.3	33.8	

* Admitting primary cardiac diagnosis ** AACVPR risk stratification for acute risk of exercise complications ns=non-significant

3.5.3 Clinical Events

In the 2-years following initiation of therapy, a total of 31 and 32 clinical events were documented in the 3-month and 12-month intervention arms respectively. Table 3.5 summarizes clinical events between groups over the first year, second year of follow-up and overall. A greater number of coronary artery bypass grafts (CABG) and non-fatal myocardial infarctions (MI) were observed in the 3-month group. While a greater number of percutaneous coronary interventions (e.g. angioplasty, stent, endarctorecotomy) were documented in the 12-month group. Over the 2-year follow-up period, one CVD death was documented in the 3-month group and three CVD deaths were observed in the 12-month group.

Table 3.5: Clinical Cardiac Events between intervention groups over year 1, year 2, and overall

	Year 1		Year 2		OVERALL		
Event	**Standard**	**Distributed**	**Standard**	**Distributed**	**Standard**	**Distributed**	**p-value**
CABG*	4	3	4	2	8	5	ns
PCI**	10	14	7	6	17	20	ns
Non-Fatal MI***	2	0	2	0	4	0	ns
Fatal MI	0	2	0	0	0	2	ns
CVD Death	1	3	0	0	1	3	ns
Non-CVD Death	0	0	1	1	1	1	ns

NOTE: Several patients under went more than one procedure *CABG= Coronary artery bypass graft surgery ** PCI= Percutaneous Coronary Intervention *** MI = Myocardial infarction CVD= Cardiovascular

3.5.4 COSTS

3.5.4.1 Program Delivery Costs

Total direct program delivery costs for each of the intervention groups and the incremental difference between groups are summarized in table 3.6.1. Due to differences in the sample size between groups total direct costs may mis-represent actual differences between groups. The mean direct per patient costs are presented in Table 3.6.2. The 12-month intervention arm possessed an incremental total direct cost of $6,880.03 and an average per patient cost $ 82.33. The largest differences in program delivery costs between groups was noted to be the cost of counseling sessions with professional staff, followed by medical consultation with the cardiac rehabilitation physician.

Table 3.6.1: Total Direct Costs of Rehabilitation Program Delivery ($CDN 2002)

Program Components	Standard (a) N=156	Distributed (b) N=150	Difference (b-a)
Professional Staff Time			
Exercise sessions	$25,455.73	$21,813.92	($3,641.81)
Contact Person Visits	$14,564.82	$15,373.36	$ 808.54
Counseling Sessions	$15,442.78	$21,025.93	$5,583.15
Medical Consults	$34,260.60	$35,870.50	$1,609.90
Stress Management	$3,601.80	$5,762.88	$2,161.08
Equipment	$7,676.52	$7,457.13	($ 219.39)
Operating costs	$7,458.02	$8,036.58	$ 578.56
Total	**$108,460.27**	**$115,340.30**	**$6,880.03**

Table 3.6.2: Mean Direct Costs of Rehabilitation Program Delivery ($CDN 2002) Per Patient

Program Components	Standard (a) N=156	Distributed (b) N=150	Difference (b-a)	p-value
Professional Staff Time				
Exercise sessions	$ 144.21	$ 144.41	$ 0.20	ns
Contact Person Visits	$ 98.61	$ 97.47	($ 1.14)	ns
Counseling Sessions	$ 99.32	$ 139.41	$ 41.18	.049
Stress Management	$ 22.80	$ 37.67	$ 15.33	ns
Medical Consults	$ 220.07	$ 237.40	$ 19.52	ns
Equipment	$ 49.30	$ 49.37	$ 0.07	ns
Operating costs	$ 47.76	$ 53.38	$ 5.77	ns
Total	**$ 681.07**	**$ 759.11**	**$ 82.33**	**.032**

3.5.4.2 Health Care Use

The total direct cost of health services use is presented for each of the major cardiac service categories in Table 3.6.3. Differences in the total health care cost are directly associated with differences in the sample size between intervention groups. The mean per patient savings derived from the 3-month program is $57.14 (See Table 3.6.4). The largest difference between health care costs between groups was unspecified hospitalizations (i.e. patient noted length of stay but not reason for hospitalization).

Table 3.6.3: Direct Costs of Health Care Services Use ($CDN 2002)

Category	Standard (a) N=156	Distributed (b) N=150	Difference (b-a)
Hospitalizations			
CABG	$88,200.00	$63,000.00	($25,200.00)
PTCA	$67,692.00	$74,510.00	$6,818.00
MI	$10,927.80	$10,927.20	($0.60)
Other Cardiac*	$20,752.80	$29,734.30	$8,981.50
Unspecified**	$83,250.00	$110,075.00	$26,825.00
Emergency Visits	$3,453.45	$3,289.00	($164.45)
Cardiac Diagnostic	$40,372.01	$48,638.18	$8,266.17
Physician Services			
General Practitioner	$123,844.50	$108,240.75	($15,603.75)
Cardiac Specialist	$126,504.00	$106,848.00	($19,656.00)
Other Specialists	$129,417.75	$121,014.00	($8,403.75)
Total	**$694,414.31**	**$676,278.03**	**($18,136.28)**

Table 3.6.4: Mean Direct Costs of Health Care Services Use ($CDN 2002) Per Patient

Category	Standard (a) N=156	Distributed (b) N=150	Difference (b-a)	p-value
Hospitalizations				
CABG	$ 565.38	$ 420.00	($145.38)	ns
PTCA	$ 433.92	$ 496.73	$ 62.81	ns
MI	$ 70.05	$ 72.85	$ 2.80	ns
Other Cardiac*	$ 133.03	$ 198.23	$ 65.20	ns
Unspecified**	$ 533.65	$ 733.83	$ 200.18	ns
Emergency Visits	$ 22.14	$ 21.93	($ 0.21)	ns
Cardiac Diagnostic	$ 258.79	$ 324.25	$ 65.46	ns
Physician Services				
General Practitioner	$ 793.86	$ 721.61	($ 72.25)	ns
Cardiac Specialist	$ 810.92	$ 712.32	($ 98.60)	ns
Other Specialists	$ 829.60	$ 806.76	($ 22.84)	ns
Total	**$4,451.38**	**$4,508.52**	**$ 57.14**	**ns**

***Other cardiac: Hospital admission for angina, heart failure, arrhythmia, AAA, pacemaker implant, cardio version**
**Unspecified: Hospital days reported with unspecified reason for admission (valued using UOHI hotel costs)

3.5.5 Utilities and Quality Adjusted Life Years

3.5.5.1 TTO Utilities

The mean time trade-off scores for intervention groups and differences between groups over the 2-year follow-up period are presented in Table 3.7.1. The mean trade-off scores adjusted for baseline differences are presented in Table 3.72.

Table 3.7.1: Mean Time Trade-off Scores for the intensive (3-month), distributed (12-month) program, and differences between groups over time

	Standard (a)	Distributed (b)	Difference (b-a)	p-value
Baseline	0.8305	0.8128	-0.0177	ns
3-months	0.8832	0.8815	- 0.0017	ns
6-months	0.8875	0.8904	0.0028	ns
12-months	0.8938	0.8913	-0.0025	ns
15-months	0.9125	0.8834	-0.0291	ns
24-months	0.8951	0.8005	-0.0946	.002

Table 3.7.2: Mean change in observed time trade-off scores (adjusted for baseline differences)

Time Trade-Off Index	Standard (a)	Distributed (b)	Difference (b-a)	p-value
3-months	0.0527	0.0704	0.0177	ns
6-months	0.0586	0.0784	0.0198	ns
12-months	0.0648	0.0793	0.0145	ns
15-months	0.0833	0.0715	-0.0118	ns
24-months	0.0660	-0.0108	-0.0768	.03

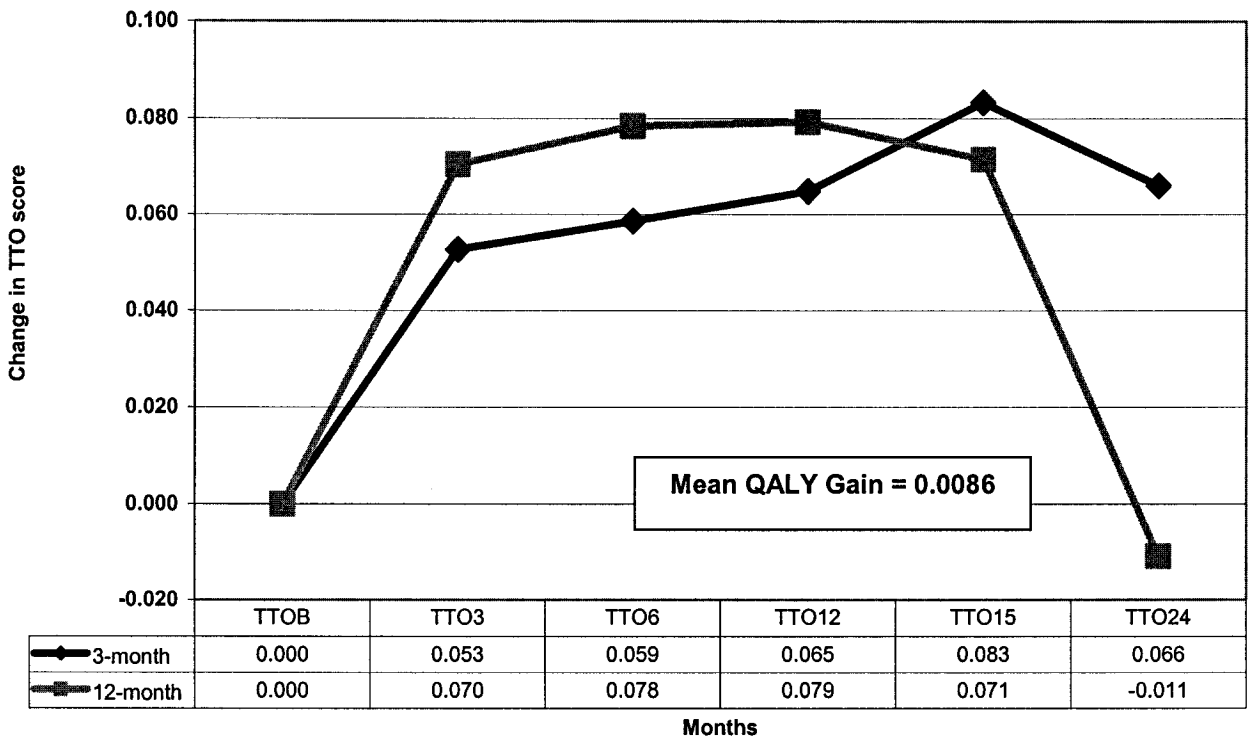
3.5.5.2 Quality Adjusted Life Years

Table 3.7.3 summarizes the mean quality of life year (QALY) gained for the intervention groups and the incremental mean QALY gain between groups at 2 years. The mean gain between intervention groups at the end of year 2 was 0.009 greater in the 3-month intervention arm as compared to the 12-month group. Figure 3.3 provides a graphical representation of time trade off scores used to calculate the area under the curve for the mean quality adjusted life year gained 2 years following initiation of CR.

Table 3.7.3: Mean quality adjusted life years gained (adjusted for baseline differences) at 2-years calculated using the area under the curve method

Index	Standard (a)	Distributed (b)	Difference (b-a)
Delta QALY (2yr)	0.0618	0.05318	- 0.0086

Figure 3.3: Mean Time-Trade-off Scores for the standard and distributed intervention arms over 2-years adjusted for Baseline Differences



	TTOB	TTO3	TTO6	TTO12	TTO15	TTO24
3-month	0.000	0.053	0.059	0.065	0.083	0.066
12-month	0.000	0.070	0.078	0.079	0.071	-0.011

3.5.6 Incremental Cost-Utility

Incremental cost-utility ratios were calculated for the end of year 1 and year 2. The cost per QALY gained was $16,228 at the end of two years in support of the 3-month intervention arm. Table 3.8.1 summarizes the incremental cost, QALYS gains, and cost-utility ratio.

Table 3.8.1: Estimates of incremental costs (CDN 2002), quality adjusted life years (QALYs), and cost/QALY gained with the 12-month cardiac rehabilitation group at year 2 using differences in the time trade-off (TTO)

Parameter	b – a
Mean Program Delivery Costs	$ 82.33
Mean Health Care Savings	$ 57.14
Net HC Expenditures	$ 139.47
Delta QALY (2 year)	- 0.0086
Incremental Cost / QALY	($ 16,228)

3.5.7 Uncertainty

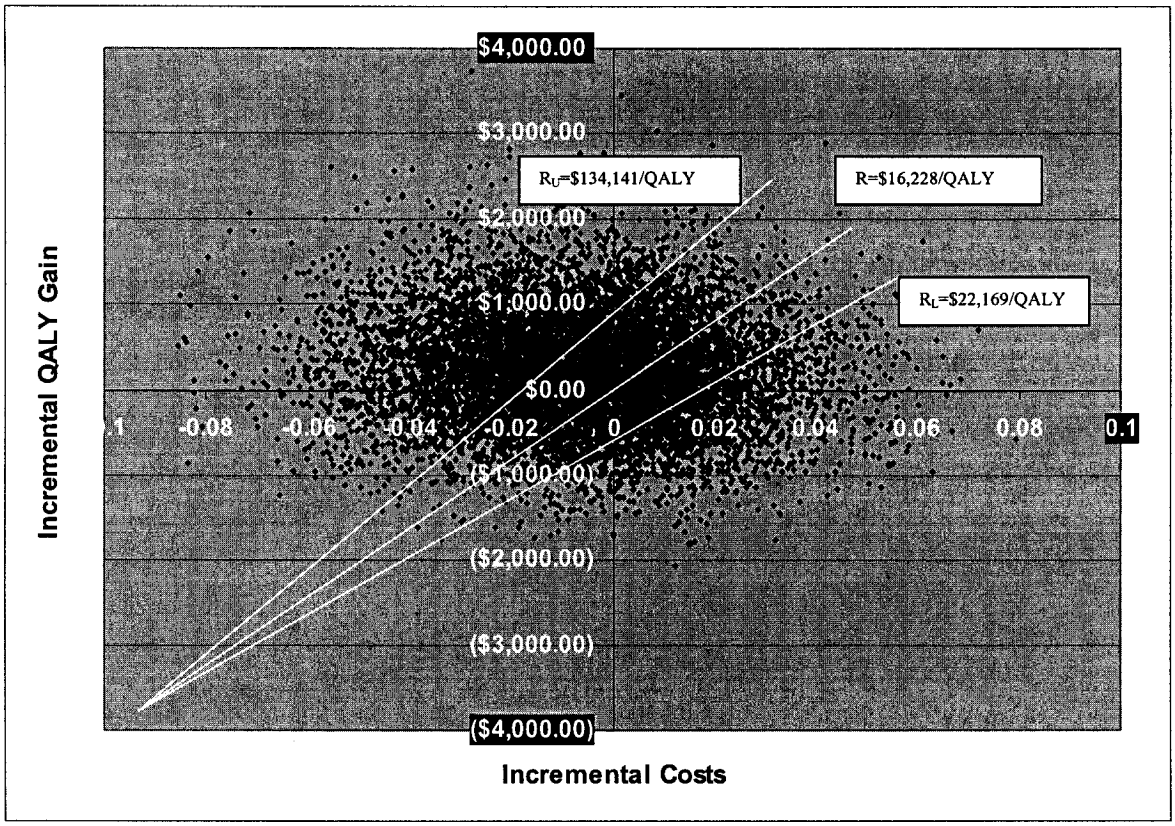
3.5.7.1 Bootstrap Confidence Intervals

Table 3.8.2 provides a summary of the mean and 95% confidence intervals for study costs, QALY gains and recalculated cost-utility ratios. The scatter-plot of incremental costs and QALY gains is displayed in Figure 3.4 based on the bootstrap replications. The scatter-plot demonstrates the fact that uncertainty exists across all four quadrants of the CE plane suggesting caution should be used in the interpretation of bootstrap confidence intervals.

Table 3.8.2: Incremental Costs, mean QALY gain, and Cost/QALY calculated for the mean, lower 2.5% and upper 97.5% Confidence Intervals at 2 years using the Bootstrap technique

Parameter	Mean	CI 2.5%	CI 97.5%
Incr. Net Costs	$ 139.47	($ 287)	$ 566
Incr. QALY (2-year)	- 0.0086	- 0.013	-0.004
Incr. Cost / QALY	($ 16,228)	$ 22,169	($ 134,141)

Figure 3.4: Scatter plot of the Bootstrap replications of the Incremental Cost and Incremental QALY Gain on the CE plane (B=10,000)



3.5.7.2 Cost-Effectiveness Acceptability Curves

Due to the difficulty in interpretation of ICUR that is introduced when the distribution of bootstrap replications falls into multiple quadrants of the CE plane a cost-effectiveness acceptability curve (CEAC) was prepared to assist with data interpretation. The CEAC was modeled based on probabilities derived from the bootstrap replications and therefore represent an estimate of the positive net benefit. Figure 3.5 displays the probability that the 12-month program will produce a positive net benefit. The CEAC displayed in Figure 3.6 indicates the probability that the 3-month program will be found more cost-effective ranges between 0.63 and 0.67. Exhibit 12 provides a summary table of the probabilities that the 3-month program was cost-effective at each of the threshold values.

Figure 3.5: Cost-effectiveness acceptability curve illustrating the probability the 12-month treatment is optimal at each monetary threshold value

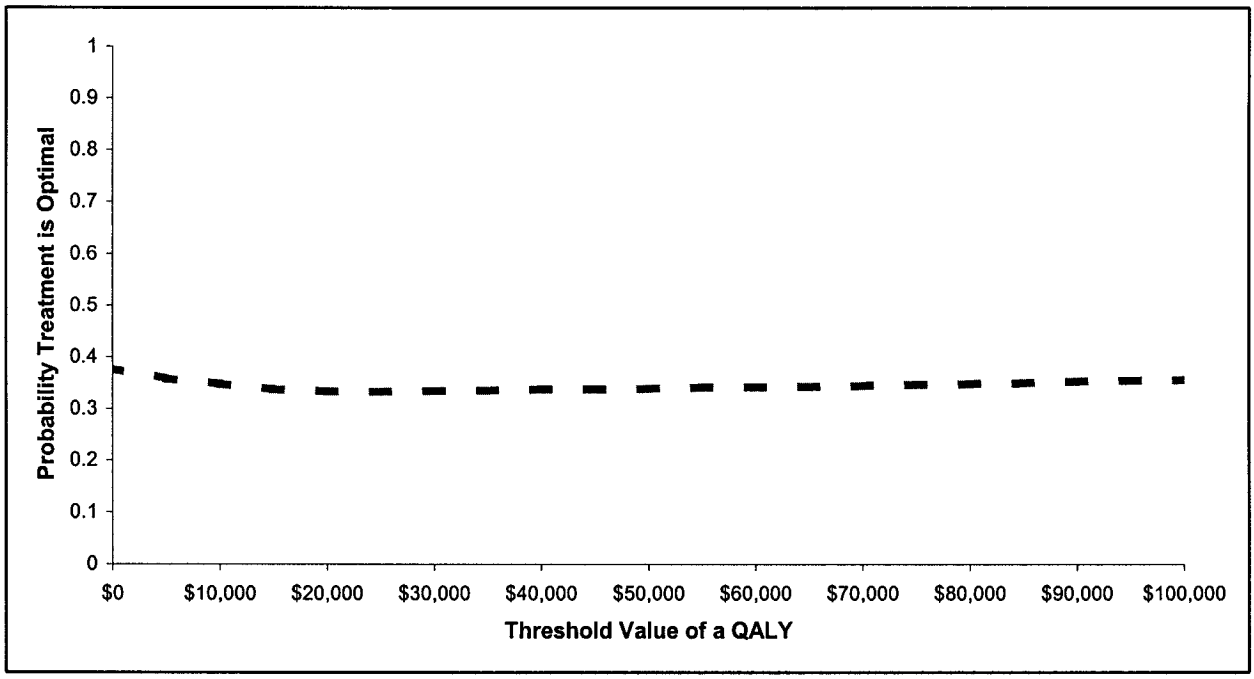
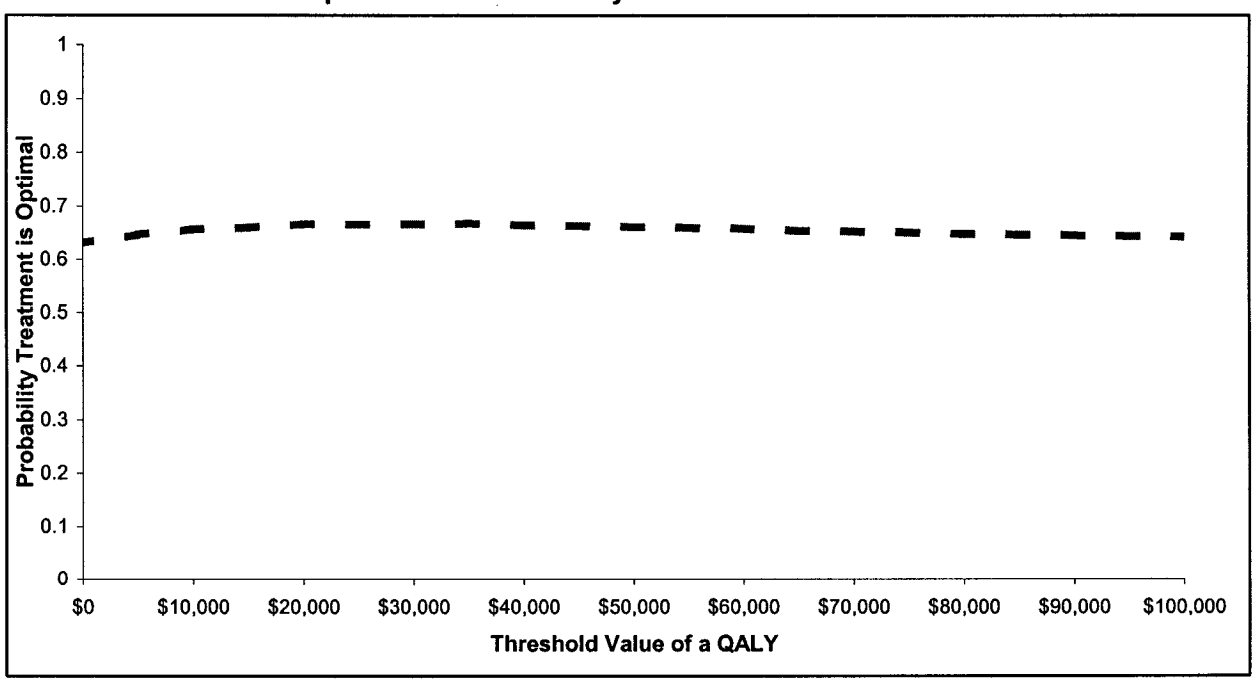


Figure 3.6: Cost-effectiveness acceptability curve illustrating the probability the 3-month treatment is optimal at each monetary threshold value



3.5.7.3 Sensitivity Analysis

Table 3.8.3 provides a summary of the incremental mean, and 95% confidence intervals for key study parameters adjusted to reflect uncertainty using probabilistic Monte Carlo simulations and the recalculated cost-utility ratios. Exhibit 13 provides a detailed summary of the recalculated means for variables adjusted within the sensitivity analyses.

Table 3.8.3: Incremental Costs, QALYs gained, and Cost/QALY calculated for the mean adjusted for uncertainty via sensitivity analysis using Monte Carlo Simulation

Parameter	Mean	CI 2.5%	CI 97.5%
Incr. Net Costs	($ 561.29)	($ 981.16)	$ 1,599.55
Incr. QALY (2-year)	- 0.01	- 0.01	-0.01
Incr. Cost / QALY	**($ 91,899)**	**$ 98,116**	**($ 159,955)**

3.6 Stratified Analysis

3.6.1 Risk Stratification

Stratified analyses were used to compare differences across cardiac risk strata using both the Canadian Association of Cardiac Rehabilitation (CACR) Guidelines and the American Association of Cardiovascular-Pulmonary Rehabilitation Guidelines (AACVPR).

The results of the stratified analysis for the CACR composite risk stratification score and sub-scales for acute risk and disease progression are presented in Tables 3.9.1 through 3.11.2. The cost-utility ratio for each strata compared has been summarized in the last column of the incremental mean cost table titled interpretation using guidelines provided by Laupacis[10, 80]. Estimates of incremental cost-utility suggest the standard 3-month program was a more cost-effective intervention for patients at higher overall risk and risk of disease progression as assessed by the CACR risk stratification tool. The 12-month program was more cost-effective for patients at lower risk of disease progression as assessed by the CACR tool. Table 3.12.1 and Table 3.12.2 display similar findings using the AACVPR risk stratification tool.

3.6.1.1 Canadian Association of Cardiac Rehabilitation (CACR) Total Risk Score

Table 3.9.1: Mean Costs, QALYs gained (adjusted for baseline differences) across CACR total cardiac risk strata for the 3-month and 12-month intervention arms at 2 years

CACR Risk Strata	N	Mean Costs	Delta QALY Gained
3-month			
Moderate	45	$ 3,269	0.0429
High	77	$ 5,704	0.0735
Very High	33	$ 6,396	0.0573
12-month			
Moderate	40	$ 5,176	0.0660
High	73	$ 5,595	0.0593
Very High	33	$ 4,549	0.0368

Table 3.9.2: Two Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across CACR total cardiac risk strata

Total CACR Risk Strata	Inc. Mean Costs	Incremental QALY Gained	Incremental Cost/QALY	Interpretation
Moderate	$ 1,908	0.0231	$ 82,582	12-month more expensive, more effective
High	$ (109)	-0.0142	$ 7,666	3-month more expensive, more effective
Very High	$ (1,847)	-0.0205	$ 90,314	3-month more expensive, more effective

3.6.1.2 Canadian Association of Cardiac Rehabilitation (CACR) Acute Risk Score

Table 3.10.1: Mean Costs, QALYs gained (adjusted for baseline differences) across CACR acute cardiac risk strata for the 3-month and 12-month intervention arms during 2-year trial

CACR Disease Progression	N	Mean Costs	Delta QALY
3-month			
Moderate	42	$ 3,360	0.0630
High	77	$ 5,352	0.0587
Very High	36	$ 6,725	0.0664
12-month			
Moderate	38	$ 5,145	0.0894
High	65	$ 5,293	0.0604
Very High	44	$ 5,290	0.0197

Table 3.10.2: Two-Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across CACR acute cardiac risk strata

CACR Acute Risk	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
Moderate	$ 1,785	0.0263	$ 67,727	12-month more expensive, more effective
High	$ (59)	0.0018	($ 33,153)	12-month Dominant (less expensive, more effective)
Very High	$ 1,434	-0.0468	$ 30,642	3-month more expensive, more effective

3.6.1.3 Canadian Association of Cardiac Rehabilitation Risk of Disease Progression

Table 3.11.1: Mean Costs, QALYs gained (adjusted for baseline differences) across CACR risk of disease progression strata for the 3-month and 12-month intervention arms at 2 years

CACR Disease Progression	N	Mean Costs	Delta QALY
3-month			
Moderate	60	$ 3,749	0.0441
High	63	$ 6,611	0.0864
Very High	32	$ 4,858	0.0461
12-month			
Moderate	50	$ 4,662	0.0803
High	69	$ 5,811	0.0396
Very High	28	$ 4,998	0.0403

Table 3.11.2: Two-Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across CACR risk of disease progression strata

CACR Disease Progression	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
Moderate	$ 913	0.03619	$ 25,224	12-month more expensive, more effective
High	$ (801)	-0.0463	$ 17,097	3-month more expensive, more effective
Very High	$ 140	-0.0058	$ (24,059)	3-month Dominant (less expensive, more effective)

3.6.1.4 American Association of Cardiovascular-Pulmonary Rehabilitation (AACVPR) Risk Stratification

Table 3.12.1: Mean Costs, QALYs gained (adjusted for baseline differences) across AACVPR cardiac risk strata for the 3-month and 12-month interventions at 2 years

AACVPR	N	Mean Costs	Delta QALY
3-month			
Low	28	$ 3,905	0.0172
Moderate	85	$ 5,230	0.0866
High	42	$ 5,751	0.0404
12-month			
Low	32	$ 3,534	0.0724
Moderate	67	$ 6,019	0.0395
High	49	$ 5,368	0.0606

Table 3.12.2: Two-Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across AACVPR risk strata

AACVPR Risk of Strata	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
Low	$ (370)	0.0552	$ (6,710)	12-month Dominant (less expensive, more effective)
Moderate	$ 789	- 0.0471	$ (16,770)	3-month Dominant (less expensive, more effective)
High	$ (383)	0.0202	$ (19,014)	12-month Dominant (less expensive, more effective)

3.6.2 Cardiac Diagnosis

Stratified analysis between referring cardiac diagnosis groups suggest the 3-month program was a cost-effective program for CABG patients (See Table 3.13.1). Differences in the estimates for incremental cost-utility ratios between MI, angina pectoris, and PCI are not significant at the $50,000/QALY threshold (See Table 3.13.2).

Table 3.13.1: Mean Costs, QALYs gained (adjusted for baseline differences) across cardiac diagnosis groups for the 3-month and 12-month groups during the 2-year follow-up

Diagnosis	N	Mean Costs	Delta QALY Gained
3-months			
MI	18	$ 5,611	0.0224
Angina	9	$ 4,415	0.0497
CABG	66	$ 4,307	0.0891
PCI	64	$ 5,988	0.0461
12-months			
MI	18	$ 7,898	-0.0286
Angina	12	$ 7,803	0.0283
CABG	70	$ 3,968	0.0793
PCI	50	$ 5,514	0.0517

Table 3.13.2: Two-Year Incremental Mean Costs, QALY gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across cardiac diagnosis groups

Cardiac Diagnosis	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
MI	$ 2,287	-0.0510	$ (44,889)	3-month Dominant (less expensive, more effective)
Angina Pectoris	$ 3,388	-0.0214	$ (158,592)	3-month Dominant (less expensive, more effective)
CABG	$ (318)	-0.0100	$ 32,589	3-month more expensive, more effective
PCI	$ (474)	0.0056	$ (84,873)	12-month Dominant (less expensive, more effective)

3.6.3 Participant Age Categories

Stratified analyses between participant age categories reveal younger (<55) and patients 65-74 years of age displayed larger mean QALY gains in the 3-month intervention group (See Table 3.14.1). Patients between the ages of 55-64 and 75 years or greater observed larger mean QALY gains and lower mean direct costs in the 12-month intervention arm (See Table 3.14.2).

Table 3.14.1: Mean Costs, QALYs gained (adjusted for baseline differences) across participant age categories for the 3-month and 12-month intervention arms during 2-year trial

Age Category	N	Mean Costs	Delta QALY Gained
3-months			
<55	59	$ 3,824	0.0737
55-64	53	$ 5,657	0.0536
65-74	38	$ 6,796	0.0691
≥75	7	$ 2,965	-0.0085
12-months			
<55	62	$ 6,587	0.0609
55-64	48	$ 4,028	0.0749
65-74	28	$ 4,924	- 0.0122
≥75	12	$ 4,263	0.0446

Table 3.14.2: Two-Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across Participant Age Categories

Age Category	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
<55	$ 2,763	-0.0128	$ (215,369)	3-month Dominant (less expensive, more effective)
55-64	$ (1,630)	0.0213	$ 76,454	12-month Dominant (less expensive, more effective)
65-74	$ (1,872)	-0.0569	$ 32,882	3-month more expensive, more effective
≥75	$ 1,298	0.0531	$ 24,430	12-month more expensive, more effective

3.6.4 Gender

Table 3.15.1 provides summary of the mean costs and QALYs for male and female study participants. Female cardiac patients were observed to have experienced significant QALY gains (+0.0845) in the 12-month group compared to the 3-month. A cost-utility ratio of $56,611 was found in the 12-month group in the sample of women. The stratified analyses with male participants indicate the standard program is superior associated with a CE ratio of $17,743/QALY (See Table 3.15.2).

Table 3.15.1: Mean Costs, QALYs gained (adjusted for baseline differences) across participant gender for the 3-month and 12-month intervention arms during 2-year trial

Age Category	N	Mean Costs	Delta QALY Gained
3-months			
Female	25	$ 5,273	0.0399
Male	129	$ 5,128	0.0662
12-months			
Female	16	$ 9,973	0.1244
Male	130	$ 4,710	0.0427

Table 3.15.2: Two-Year Incremental Mean Costs, QALYs gained, and Cost/QALY gained between the 3-month and 12-month intervention arms across Participant Gender

Age Category	Inc. Mean Costs	Inc. QALY Gained	Cost / QALY	Interpretation
Female	$ 4,701	0.0845	$ 55,611	12-month more expensive, more effective
Male	$ (418)	-0.0236	$ 17,743	3-month more expensive, more effective

Figure 3.7 provides an overview of the stratified analyses performed. The cost-effectiveness ratios favouring the 3-month group are presented on the left of the figure and those favouring the 12-month intervention arm are presented on the right.

Figure 3.7: Summary of Incremental Cost Utility Ratios from Stratified Analyses across AACVPR and CACR Cardiac Risk Strata, Cardiac Diagnosis, and Age Categories

Quadrant IV **Standard program less costly and more effective** CACR Acute – very high CACR Disease Progression – very high AACVPR – moderate MI Angina Age <55	**QUADRANT I** **Distributed Program more costly and more effective** CACR moderate CACR Disease Progression moderate Age >75 years Females
QUADRANT III **Standard program more costly and more effective** CACR high CACR very high CACR acute moderate CACR disease progression high CABG Age 65-74 Males	**QUADRANT II** **Distributed program more costly and more effective** CACR Acute – high AACVPR – low AACVPR – high PTCA Age 55-64

3.7 Sub-group Analysis

Sub-group analyses were performed in patients reporting a time-trade-off utility score of 1.0 or less at baseline. Given that the capacity for treatment effect was negligible in patients reporting TTO scores of 1.0 at baseline this analysis was conducted to assess intervention impact on patient population with potential for clinical improvement. Table 3.16 provides a summary of the group and incremental cost-utility ratios for this patient sub-group. Differences between groups were not found to be significant.

Table 3.16: Mean two-year costs, QALYs gained, and Cost/QALY in patients with a baseline Time-Trade-off score of less than 1.0

QALY <1.0	Mean Costs	QALY Gained	Cost/QALY	Interpretation
3-month	$ 6,359.84	0.1499	$ 42,435	
12-month	$ 5,994.86	0.1493	$ 40,149	
Incremental	$ 364.99	-0.0006	$ 654,697	Dominant

Sub-group analyses were performed in the sample of surviving patients over the 2-year follow-up period. The incremental cost utility analysis with the six deceased patients removed is presented in Table 3.17. The 3-month intervention was dominant ($24,878) with an estimated mean incremental QALY gain of 0.006.

Table 3.17: Mean two-year costs, QALYs gained, and Cost/QALY gained amongst surviving patients

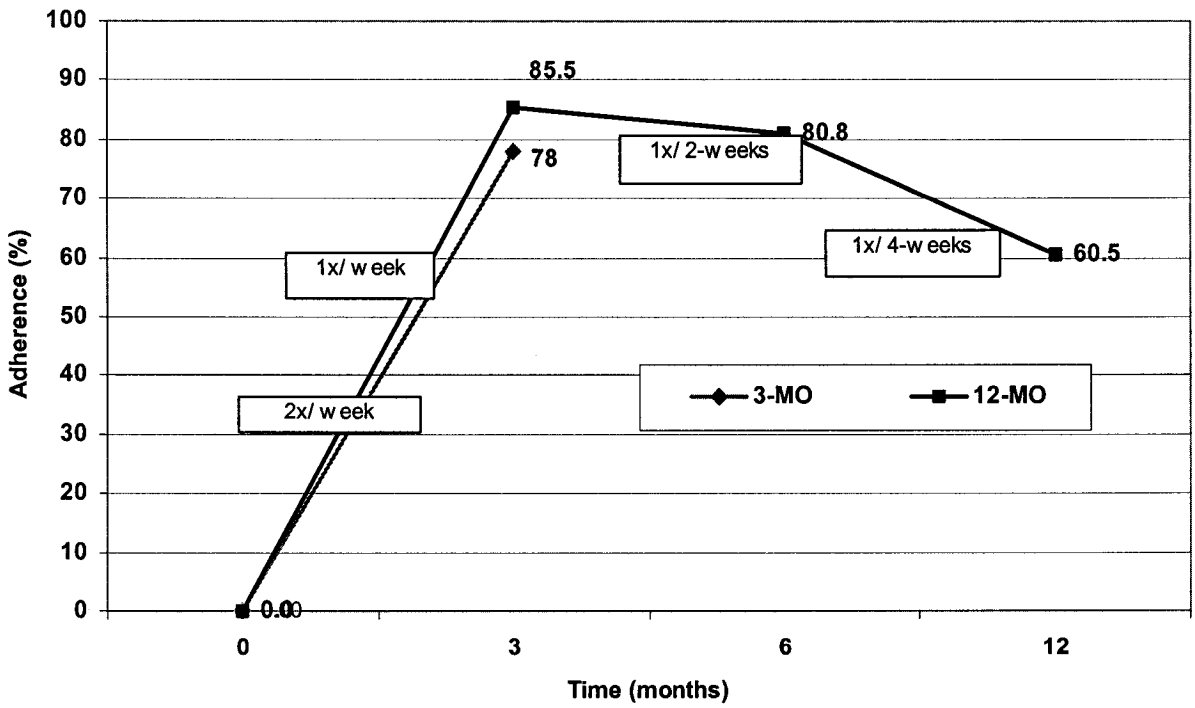
Surviving Participants	N	Mean Costs	QALY Gained	Cost/QALY	Interpretation
3-month	154	$ 4,842.18	0.0927	$ 52,214.82	
12-month	146	$ 4,992.32	0.0867	$ 57,581.13	
Incremental	300	$ 150.14	-0.0060	$ (24,877.79)	Dominant

Figure 3.8 provides an overview of the compliance with exercise treatment for the 3-month and 12-month intervention groups. Differential compliance rates with the exercise sessions were observed over the three phases of the 12-month CRP. A 20% drop in compliance was observed after 6-months of intervention when the frequency of supervised exercise sessions was reduced from bi-monthly (2 sessions per 4-weeks) to monthly (1 session per 4 weeks). Table 3.18 provides an overview of the mean cost-utility ratios for the 3-month, 12-month and incremental differences between groups 2-years following initiation of cardiac rehabilitation. In patients with compliance rates of 80% or greater the 3-month intervention arm produced larger QALY gains (+0.03) and a cost-utility ratio that is dominant ($18,974/ QALY).

Table 3.18: Mean two-year costs, QALYs gained, and cost per QALYs gained in patients with intervention compliance rates of 80% or greater

Compliance >80%	N	Mean Costs	QALYs Gained	Cost/QALY	Interpretation
3-month	120	$ 5,026.90	0.0812	$ 61,875	
12-month	113	$ 5,595.40	0.0513	$ 109,108	
Incremental	233	$ 568.50	-0.0300	$ (18,974)	Dominant

Figure 3.8: Rates of compliance with intervention protocol for the 3-month and12-month intervention groups



3.8 Discussion

3.8.1 Cost-Utility

This study is one of only two cost-utility analyses evaluating cardiac rehabilitation services and the only full prospective randomized control trial evaluation of alternative CR program delivery against standard CRP. The 3-month intervention was found to be dominant ($16,228/QALY), resulting in a lower overall cost to the health care system and larger gains in QALYs two years following initiation of CR. Confidence Intervals calculated using Monte Carlo simulation reveal differences between groups are significant at the 95% level (lower CI $22,169/QALY; Upper CI ($134,141)/QALY). The cost-utility ratio observed at the upper confidence interval remained dominant, however that observed at the lower confidence interval produced both larger costs and greater mean QALY gain for the 3-month group (Quadrant III). A probabilistic sensitivity analyses was conducted by sampling from each of the variables associated with significant uncertainty simultaneously using Monte Carlo simulation. The recalculated mean cost-utility ratio based on the sensitivity analysis continued to favour the 3-month intervention though difference between groups was small $91,899/QALY gained.
Confidence intervals calculated using the Bootstrap technique indicated that uncertainty concerned more than 1 quadrant of the CE plane (Figure 5.71). This type of uncertainty poses problems in the interpretation of confidence intervals since we are unable to differentiate between positive and negative ICER that favour the distributed 12-month treatment and those that favour the standard treatment [79]. The Cost-Effectiveness Acceptability Curves (CEAC) displayed in Figure 3.6 assists in summarizing uncertainty as a measure of the number of times the bootstrap replications fall to the left (favouring the 3-month treatment) of the cost-effectiveness plane for specific ICER thresholds summarized as a probability of a positive net benefit. The observed probability of a net benefit for the 3-month treatment ranged between 0.63 and 0.67 support the conclusion that the 3-month treatment was superior in a larger proportion of cases. Study findings suggest the experimental 12-month intervention does not provide greater benefits than the standard cardiac rehabilitation program delivery as originally hypothesized.

3.8.1.1 Program Delivery and Health Care Costs

Costs attributable to the cardiac rehabilitation program delivery were $681.07 and $759.11 for the three and twelve-month intervention arms, respectively. The main cost differentiator was the higher rate of professional one-on-one consultations conducted in the twelve-month group. The opportunity for 12-month program participants to access services over a prolonged period and the opportunity to address rehabilitation issues that arose later in the intervention period served to increase the total number of professional consultations. The mean incremental health care savings provided by the 3-month program was $57.14, (Lower 95% CI: ($355); Upper 95% CI: $480). Mean differences between groups with respect to health care use were not significant at the 95% confidence interval.

3.8.1.2 Quality Adjusted Life Years

Both intervention groups displayed a mean time-trade off (TTO) gain over the first year of follow-up. The mean QALY gain observed within groups over the 2-years was 0.061 and 0.053 for the 3-month and 12-month groups respectively. At the end of first year of follow-up the mean QALY gain adjusted for baseline differences was greater in the 12-month group. A slight drop in TTO gains in both groups was observed between year 1 and year 2. The mean 2-year QALY gain was significantly greater in the 3-month group as compared to the 12-month. Despite a greater mean baseline TTO score, when adjusted for baseline differences the mean two-year QALY gain continued to favour the 3-month intervention arm (0.009). Interestingly, 51.3% of patients reported a time-trade off score of 1.0 (full health) at baseline. Most of these patients were consistent in reporting maximal health states throughout the 2-

year follow-up period suggesting a ceiling effect is associated with the TTO in cardiac rehabilitation settings.

3.8.1.3 Stratified and Sub Group Analyses

As recommended by Torrence (1996), stratified analyses were based on variables identified a priori and are interpreted with caution [35]. Several authors have explored the role of disease risk on the cost-effectiveness of CVD interventions[66]. Stratified analyses suggest the 3-month program, was a more cost-effective intervention for patients at high risk of disease progression ($17,097/QALY), CABG ($32,587/QALY) and MI ($44,889/QALY) as well as male ($17,743/QALY) patients. The 12-month program was slightly more cost effective for patients with lower risk of disease progression ($25,224/QALY), patients older than 75 years ($24,430/QALY) and female ($55,611/QALY) cardiac patients. These results suggest patients may benefit from triage to available CR intervention models according to the risk strata, and diagnosis group into which they fall.

Sub-group analyses performed in the sub-sample of patients who reported a TTO score that was less than maximal (<1.0) supported the 3-month intervention as dominant. Dominance continued to be observed when analyses were performed in the sub-set of surviving patients ($24,878/QALY) and with patients reporting intervention compliance rates of 80% or greater. A mean QALY gain of 0.03 was observed in the sub-group analyses of highly compliant patients. This significantly greater than the mean QALY gain of 0.009 observed in the main analysis. Stratified and sub-group analyses may be compromised by insufficient sample size and must be validated by further study.

3.8.1.4 Cost-Utility Thresholds

To assist with the interpretation of incremental cost effectiveness ratios Laupacis (1992) has recommended a 4-tier grading system for classifying the relative cost effectiveness of health care services (See Table 3.19) [80]. The incremental cost-utility ratios observed in this trial falls within the highly cost-effective range (<$20.000 / QALY) [80]. Attempts by Laupacis and others to quantify the value of the maximally acceptable cost-utility ratio have received wide-spread criticism. This is in part due to the arbitrary nature of such cut-offs, the inconsistency such thresholds hold when attempting to maximize outcomes from fixed health care budgets, and even the effect of the time value of money [79]. In a recent publication, Laupacis suggests that given the time value of money a CE ratio of less than $50,000 can be considered attractive and may serve as a more relevant threshold [81]. While there is no universally accepted guideline for ranking the relative cost-effectiveness of competing health care interventions these guidelines can assist with comparing observed CUA ratios with what is generally considered acceptable.

Table 3.19: Classification of Incremental Cost-Effectiveness Values (Laupacis, 1992)

Cost / QALY	Classification
Less than $20,000	Highly cost effective
$20,000 and $40,000	Relatively cost effective
$40,000 and $60,000	Borderline
Greater than $60,000	Expensive

3.8.2 Comparability with other cardiac interventions

Olrdridge (1993) conducted the only other cost-utility analysis of cardiac rehabilitation services [29]. In this study an 8-week cardiac rehabilitation intervention was compared against a standard care control group. A mean gain of 0.052 QALYs was reported based on time-trade off scores one year following initiation of cardiac rehabilitation compared to standard care. In the present trial a smaller incremental mean QALY gain was observed 0.009 between intervention arms. This finding is not surprising given

the current intervention sought to compare to active interventions. The mean cost of the CR intervention in the Oldridge trial was $570 (CDN 1987) which is comparable to program delivery costs ($681 and $759) observed in the present trial. In the Oldridge trial, costing was only performed for health care services where a significant difference in utilization rates between groups was observed. As such the only service assigned a cost value was other rehabilitation visits. The $9,200/QALY is in a comparable range to that observed in this trial when comparing two alternative program delivery models.
Table 3.20 provides a summary of the cost-utility ratios of CVD interventions including the cost per QALYs for CABG, PTCA, and pharmaceuticals. While the comparison table is useful to clinicians and researchers in placing the findings of the current study into perspective, we caution against direct comparisons between trials given the heterogeneity in the study designs of the noted trials including time horizons, perspectives, and patient populations.

Table 3.20: Comparison of the Cost-Utility Ratios (Cost/QALY) of various Cardiovascular Interventions valued in the year and currency of publication and CDN (2002) and USD (2002)

Intervention	Comparator	Cost/QALY	Cost/QALY 2002 CDN* 2002 USD*
Standard (3-MO) CR	12-MO CR	CDN ($16,224) (2002)	CDN ($16,224) USD ($ 10,373)
8-week CR (in mildly to moderately depressed MI patients) [29]	Standard care	USD $ 9,200 (1991)	CDN $ 23,736 USD $ 15,176
Coronary artery angioplasty (one vessel, severe angina) [32]	Medical care	USD $ 8,700 (1993)	CDN $ 22,816 USD $ 14,588
Coronary artery angioplasty (one vessel, mild angina) [32]	Medical care	USD $126,000 (1993)	CDN $330,448 USD $211,276
Captopril (in 50 year old patients surviving MI) [82]	No Captopril	USD $76,000 (1998)	CDN $221,548 USD $141,649
Coronary artery bypass graft (left main disease) [83]	Medical care	USD $ 7,900 (1991)	CDN $ 10,382 USD $ 13,032
Coronary artery bypass graft (1-vessel disease in patients with mild angina) [83]	Medical care	USD $68,200 (1991)	CDN $175,962 USD $112,503

*** 5% Discount Rate Applied**

3.8.3. Strengths and Limitations

This trial marks the first prospective trial to include non-MI subjects (CABG, PTCA, Angina) thereby increasing the generalizability of study findings to the current composition of cardiac rehabilitation patients. This study is one of only two cost-utility analysis evaluating cardiac rehabilitation services. We have also produced the first full prospective evaluation of alternative cardiac rehabilitation delivery models. The trial utilizes best practices in economic design and analysis thereby adding to the quality of published literature surrounding the economic viability of cardiac rehabilitation services.
There are potential sources of bias in the study findings. Approximately 33% of data was missing at the end of two years as a result of loss to follow-up. A slightly greater loss to follow-up rate was seen in the 12-month group upon completion of the active intervention (i.e. after year 1) as compared to the 3-month group. This differential rate of loss to follow-up introduces bias to the study's findings. A significantly larger dropout rate was observed amongst female participants (21% in males vs. 36% in females). The representation of women in the present trial is limited by the relatively large dropout rates observed amongst female patients. The present analysis was based on the sample of 306 active study

participants. The use of the active study sample for data analyses was based upon the significant uncertainty associated with estimating health care services use in non-active participants as well as the effect inclusion of inactive participants upon the baseline TTO score. Exhibit 6 provides an overview of the data analysis results when based on the 396 randomized patients.

The lack of a comparative control group minimizes the ability of this trial to determine if differences between intervention groups are greater than that which may have been observed compared to a standard care control. This study is also not able to add new evidence to support the cost-effectiveness of cardiac rehabilitation services as compared to standard care.

The 3-month (33-session) cardiac rehabilitation program was designed to resemble the most common format of cardiac rehabilitation program delivery in North America. The 12-month program was selected for inclusion based on theoretical soundness. It is possible that a different schedule or program duration may have yielded a different result. The observed drop in compliance in the 12-month group after 6-months suggests the frequency of contact in this final program phase was not well received by patients and may have had an impact on study outcomes.

The generalizability of study findings may also be limited by the fact that this study was set in a large tertiary care centre in Canada. The medical practices and service delivery models may differ from that observed in other international centers. The fact that the Canadian health care system is funded through federal and provincial governments is significantly different than that observed in other countries such as the United States. In the United States cardiac rehabilitation services and health care expenditures would be borne through a combination of government, patient, and third party insurers.

The validity of applying these results to different health care settings and systems is not clear.

The time horizon of this study was limited to the two-years following initiation of CR intervention. Unlike surgical interventions such as CABG, which incur large up-front costs result in immediate benefits, prevention programs have a lower uniform cost and delayed benefits [11]. Since prevention programs tend to produce benefits over an extended time horizon, a longer follow-up period may have produced different results. The differences observed in the mean QALY gain between year 1 and 2 of follow-up in the current trial supports this hypothesis.

3.9 Conclusions and Recommendations

3.9.1 Conclusions

Study findings suggest the experimental 12-month intervention does not provide greater benefits than the standard cardiac rehabilitation program delivery model as hypothesized. Important differences were noted in the cost-effectiveness of interventions across cardiac risk strata and diagnosis groups, suggesting patients may benefit from triage to available CR intervention models. The development and evaluation of alternative CR delivery models has the potential to assist in more effectively spending cardiac rehabilitation dollars and improving CE. This study is one of only two cost-utility analysis evaluating cardiac rehabilitation services and the only full prospective economic evaluation of alternative CR program delivery models.

3.9.2 Implications to Practice

CEA is intended to improve clinical practice and assist in the development of clinical guidelines and health policy by providing information about the value of alternative health interventions in specific populations [10]. As responsible clinicians we use health economics to guide the design and dissemination of cost-effective program models. CEAs are not intended to be the sole basis for resource allocation in health care because of the limitations of CEA methodologies and practical considerations involved in resource allocation. In addition to CEA findings, factors such as the opportunity to expand reach to cardiac rehabilitation services, reduce waiting times, and ensure hard to reach patient groups receive services should be considered. The present study has offered a number of findings, which are relevant to clinical practice in field of cardiac rehabilitation and the design of cost effective intervention models. Key implications are highlighted below;

3.9.2.1 Best Candidates for Cardiac Rehabilitation

The findings of this study suggest that patients may benefit from triage to available service delivery models. The 12-month intervention was found to provide greater cost-effectiveness to specific segments of the cardiac rehabilitation population. The cardiac patient population displays significant heterogeneity and may benefit from the availability of several program delivery models which can be tailored to the need of particular patient segments. Offering patients a pallet of efficacious service delivery options may result in improved compliance and greater cost-effectiveness. There is an opportunity to develop evidence-based triage rules to match patients to the most cost-effective service delivery models, based on factors such as diagnostic group, risk strata, age, as well as patient preference, and geographic location.

3.9.2.2 Intervention Compliance

Factors which effect intervention compliance may also influence the cost-effectiveness associated with the treatment. In the present trial, we observed a significant drop in compliance in the distributed program following the 6-month of intervention. Twenty percent of patients did not return to CR when exercise class frequency was dropped from twice monthly to once monthly. Quantitative interviews with patients revealed the once monthly exercise frequency has limited appeal and utility for many patients who had established an exercise routine outside the rehabilitation setting, and was not sufficient to assist with overcoming barriers to regular activity or dietary change in patients who had not established these practices at the end of the first 6-months. The once monthly contact frequency appears to have crossed a minimal frequency threshold. The reduction in compliance in the later 6-months of the distributed program may provide some insight into the drop in QALY gained after year 1. Strategies for improving patient compliance with intervention may assist in improving overall cost-effectiveness.

3.9.2.3 Dose Response

In addition to intervention compliance the frequency and timing of intervention contacts is hypothesized to have differential effects on program outcomes and cost-effectiveness. The findings of this study suggest that early intensive program contacts may be the best means for improving quality of life outcomes and reducing program delivery costs. Further reductions in the length rehabilitation contacts may produce additional cost effectiveness. It will be important to determine if there is a threshold exists regarding the minimum number of contacts required to produce equivalent gains. Patient groups may also have differing program contact needs. Maintaining contact beyond the standard 12-week has been noted to be particularly beneficial to elderly patients, whose PA levels is naturally less than younger patients [84].

Many alternative program delivery models have utilized less intensive program delivery models and emphasize a shift towards home-based models. The distributed (12-month) program delivery model assessed in the present investigation required participants to conduct the majority of their exercise outside the supervised cardiac rehabilitation program to meet activity targets. In many cases, cost shifting from the rehabilitation program to the patient occurs when less intensive interventions are employed.

3.9.2.4 Follow-up and Maintenance

As part of the study current study protocol, patients in both groups received regular follow-up assessments at 3, 6, 12, 15 and 24 months. We hypothesize that the follow-up assessments may have played a role in maintaining compliance levels in both groups. Other authors have noted the value of periodic follow-up to ensure the preservation of initial gains developed through cardiac rehabilitation [67]. It is difficult to assess the impact the follow-up assessments may have had on program participants. Qualitative interviews with study participants were able to establish a relationship between study follow-up assessments and motivation to remain compliant with intervention goals. An early intensive cardiac rehabilitation intervention that is followed by a maintenance follow-up intervention may be the most efficacious and cost-effective method for improving patient outcomes.

3.9.3 Suggestions for Future Research

3.9.3.1 Cost Utility of Alternative Program Delivery Models

This study is one of only two cost-utility investigations of cardiac rehabilitation interventions conducted to date. Our study is also the only prospective evaluation of alternative cardiac rehabilitation service delivery models. We have evaluated a standard 3-month versus a 12-month rehabilitation program. Several other program delivery models may be viable alternatives. Additional trials evaluating the dose response relationship required to produce clinical effectiveness and greater cost effectiveness are required.

The exploration of alternative service delivery models including home-based, telephone-based, and Internet-based CR programs will add to our knowledge of how best to treat patients. These alternative program delivery models may provide opportunities to reach more people in a potentially cost-effective manner. These alternative delivery modes generally require fewer resources (professional, equipment, facility) but have not been evaluated regarding the return on the program delivery investment.

3.9.3.2 Maintenance

Further research in needed to determine the role of follow-up in the maintenance of cardiac rehabilitation. Given that shorter more intensive delivery model appears to be the most viable program

delivery model. Methods for promoting adherence to exercise and other lifestyle behaviours after program completion will need to be developed.

3.9.3.3 Best Candidates

Identifying the "best candidates" for cardiac rehabilitation has intrigued researchers in the field of cardiac rehabilitation. As an adjunct, determining best candidates for various cardiac rehabilitation service delivery models can assist in more appropriately triaging patients to both efficacious and cost-effective programs. Stratified analyses conducted as part of this trial have detected important difference in the relative cost effectiveness produced by different CR delivery models across cardiac diagnosis. This study is one of the few studies to include non-MI patient populations. Further investigation is needed to support our understanding of how patient characteristics affect CE and which patient candidates are best suited to available program delivery models.

3.9.3.4 The Female Cardiac Patient

A significant intervention dropout rate was observed amongst female study participants. These observations support the findings of other studies indicate that compared to men eligible women are more likely to drop out and fail to complete CRP [53]. Lower self-efficacy (confidence in ones ability to engage in physical activity) and functional capacity have been documented in female cardiac patients at baseline. Women report the need to avoid pain while exercising, flexible hours, choice in exercise [53]. Current program delivery models may not be well matched to the needs of the female cardiac rehabilitation patient. While significant research has been conducted to determine why women dropout there is limited investigation and experimental trials exist regarding how best to design cardiac rehabilitation programs so as to increase enrollment, compliance and reduce dropout.

3.9.3.5 QALY Valuation

Effectiveness plays a larger role than costs in determining the CE of health care services. There is a need to look to improving the methodological rigor which utilities are measured [85]. Utility measures such as the time trade-off are designed to evaluate general health and are not disease specific (cardiac health). Current gold standard direct cost-utility measures are challenging to administer and subject to responder bias. The sensitivity of these tools to the quality of life changes gained from cardiac rehabilitation services is uncertain. The relative sensitivity of available tools for detecting change within cardiac patient populations is also not known. A ceiling effect was observed with the TTO scores reported early in the intervention period. There is a need to evaluate and develop new tools for quantifying the effects of cardiac interventions. As part of a sub-study analysis we have investigated a new preference-based utility index (the SF-6D). The SF-6D is derived from the short form health outcomes survey (SF-36) and is relatively easy to administer. The SF-6D is suggested to provide greater sensitivity to quality of life change at the upper end of the utility scale and may be more sensitive for detecting change produced by cardiac rehabilitation interventions. Chapter 3 of this Master's thesis submission has addressed the need for further validation of the SF-6D by conducting the first comparative study between the TTO and SF-6D. Further investigation is required comparing the SF-6D scores to gold standard measures and within cardiac populations before its use can be recommended. Research into additional preference based measures and scoring systems for generating utility scores from existing tools will add to the field of health economics and set the stage for future economic evaluations of cardiac rehabilitation and other cardiac interventions. To the date thresholds for meaningful TTO gains have not been established to assist with assessing the significance of study findings. Additional investigation into the quantifying clinically meaningful utility differences will add to our ability to interpret and compare CUA findings.

Chapter 4:

Comparison of the Time-Trade-Off and SF-6D Utility Measures in a Sample of Cardiac Rehabilitation Patients

EXECUTIVE SUMMARY

BACKGROUND: Cost-utility analyses are increasingly being used to assess the value of competing health care interventions. The purpose of this study is to evaluate the comparability of utility scores derived through the TTO utility measure and SF-6D preference based index; and examine the implications of difference in utility scores on the calculation of quality adjusted life years and the cost-utility ratios of two competing cardiac rehabilitation interventions.

METHODS: Study participants completed time-trade off interviews and SF-36 surveys at baseline 13, 26, 52, 65, and 104 weeks after program intake. Mean, standard deviation, and 95% confidence intervals were calculated for utility scores derived from the SF-6D and TTO methodologies. With-in subject differences in the mean utility score were tested by paired t-test and distributions were evaluated by histogram. Correlations statistics were calculated between the SF-6D and TTO utilities across time-points and displayed as scatterplots. Incremental quality adjusted life years and cost-utility ratio were calculated as the difference utilities derived from the SF-6D and TTO.

RESULTS: A total of 371 patients completed TTO and SF-6D measures at the baseline evaluation. The mean baseline utility score for the TTO and SF-6D was 0.80 and 0.67 respectively. A difference of -.129 (LCI -.1545 - UCI .1026, $p<0.001$) was observed between measures. . Correlations between the instruments ranged between 0.323 at baseline and 0.549 at 24-months ($p<0.001$). The mean QALY gain between groups was 0.175 and 0.022 as derived from the SF-6D and TTO. A cost-utility ratio of $7,326/QALY gained was calculated based on the SF-6D as compared to a ratio of $5,950/QALY using the TTO.

CONCLUSION: In conclusion, the SF-6D may be well suited to the assessment of HRQL in cardiac populations given its ability to discriminate among small difference at the upper end of the utility scale. Further investigation is required comparing the SF-6D against gold standard measures and within cardiac populations before it can be recommended as the preferred method for deriving utility scores.

4.1 Introduction

Cost-utility analyses are increasingly being used to assess the value of competing health care interventions. Cost utility analyses describe effectiveness in terms of the cost per quality adjusted life year (QALY). QALYs serve as a measure of both quantity of life and quality of life by ranking health status on an interval scale from 0 representing death and 1 representing optimal health [75]. QALYs are derived through preference utility measures by either direct measurement or, indirectly, by means of multi-attribute health-utility systems [75]. Direct methods of measuring utilities include, the Standard Gamble (SG) and Time-trade-off (TTO). Both are interview-based methods in which respondents are asked to choose between alternative health state outcomes. These direct measures have been criticized regarding the complexity of their interview based administration and difficulty encountered by patients in processing alternatives. The use of life and death decisions within these measures has been suggested to provide an unrealistic representation of most health care decisions. Furthermore, factors such as personal and religious beliefs, risk attitude, and time preferences will influence a respondent's preferences [86, 87].

Several multi-attribute utility measures have been developed which serve as generic preference-weighted health state classification systems that can be used for generating utility scores. These systems generally include questions, which evaluate health state dimensions, and an algorithm based scoring system for calculating a utility score. The EuroQoL (also known as the EQ-5D) and the Health Utilities Index (HUI) are amongst the most popular multi-attribute health state valuation systems. Recent work by Brazier has resulted in the development of a preference-based index derived from the Medical Outcomes Short Form (SF-36) survey. The SF-36 health related quality of life questionnaire is widely used in the evaluation of health care interventions. The SF-36 quality of life sub-scales and composite scores have been validated in healthy and diseased populations and are found to be sensitive to changes in health status resulting from cardiac interventions, including investigations of cardiac rehabilitation [6, 88, 89]. It is hypothesized that the SF-6D index may be a more robust measure of heath state status due to the large size of its descriptive system as compared to other multi-attribute systems [90].

There have been relatively few studies, which have systematically compared between different methods for calculating utilities. In a recent study, the SF-6D was found to produce systematically higher utility scores than the EQ-5D and HUI [91]. Trials evaluating the SF-6D against the EQ-5D (correlation coefficient of 0.7691, $P<0.001$) concluded that the SF-6D does not describe health states at the lower end of the utility scale but is more sensitive than the EQ-5D is detecting small changes in the upper end of the scale [92, 93]. A recent comparison between the SF-6D and the HUI ($r= 0.58$ CI 0.48-0.68) found poor agreement between utility scores derived from these methods [94]. The authors suggest likely differences between these measures are due to differences in underlying health concepts being measured.

To date, no study has compared the SF-6D against the TTO direct utility measure. The purpose of this study is to evaluate the comparability of utility scores derived through the TTO utility measure and SF-6D preference based index and assess potential gains in QALYs and the associated cost-utility ratio in a sample of cardiac rehabilitation patients.

4.2 METHODS

4.2.1 Study Design

Data utilized in this comparative evaluation was collected from a large randomized control trial comparing the incremental cost-utility of two alternative program delivery models. A total of 392 patients with Coronary artery disease who consented to study participation were randomized to either a standard 3-month program were compared to a distributed 12-month program. Time trade-off interviews and SF-36 surveys were complete with study participants at baseline 13, 26, 52, 65, and 104 weeks after program intake via questionnaire and face-to-face interview.

4.2.2 Main Outcome Measures

4.2.2.1 Time Trade-off

The TTO is a direct utility measurement that was developed based on the SG utility but designed to consider patient face validity when evaluating health trade-offs. The technique consists of a TTO question that is prefaced with a visual analog scale ranking of current health status. The visual analog scale is a 100-point scale with anchors of death and perfect health. Patients are asked to indicate their current health state as a percentage on this scale. The TTO question asks subjects to consider an average life expectancy for a person their age and indicate how many years of life they would be willing to give up to be in perfect health. The TTO follows a ping-pong methodology in which a subject's response to a question leads to a second TTO question with new parameters. The time period of full health is varied until the respondent is indifferent between the two alternatives. The preference score is determined by a ratio between the number of years (x) a patient is willing to spend in the indifferent health state over the total number of years of life expected for his/her age (t) (i.e. x/t) [11]. Preference weight values are on a 0 (death) to 1.0 (full health) scale. The TTO has been applied in clinical studies, economic evaluations, and the measurement of population health [75-77]. The TTO was selected because is simpler for respondents to comprehend as compared to the SG despite the fact that the scores generated are not true Von Neumann-Jorgensen Utility scores[11].

4.2.2.2 SF-6D Health State Classification

A second set of Utility scores will be calculated via the SF-6D index. The SF-6D is a simple multi-attribute preference based health state classification system based on the popular Medical Outcomes Short Form-36 (SF-36) health related quality of life instrument [76, 90, 95]. The SF-6D algorithms were derived using the Standard Gamble utility measure. The SF-6D is a relatively new classification system and has had limited use in cardiac populations. Ten items from the SF-36 are used to calculate the six dimensions of the SF-6D and the composite index. The SF-6D has six dimensions ($\delta = 1,2,\ldots,6$), each with between two and six levels (λ). The six SF-6D dimensions are; physical functioning, role limitations, social functioning, pain, mental health, and vitality.

4.2.3 Statistical Analysis

Patient data was converted into TTO and SF-6D utility scores based upon the scoring algorithms from Torrence [96] and Brazier et. al. [95]. Descriptive statistics for the entire sample were computed along with mean, standard deviation, and 95% confidence intervals for utilities. With-in subject differences in the mean utility score were tested by paired t-test and distributions were evaluated by histogram. Pearson correlation coefficient was computed between measures, as well as, Kendall's Tau to account for the possibility of ties between ordinal rankings.

We also evaluated the effect of the utility measures in the calculation of QALYs and the resulting incremental cost-utility ratio. QALYs were calculated using the area under the curve method and adjusted to reflect baseline differences for the standard and distributed intervention groups. The

incremental cost-utility ratio was calculated as the difference in the mean cost divided by the mean incremental QALY gained.

4.3 RESULTS

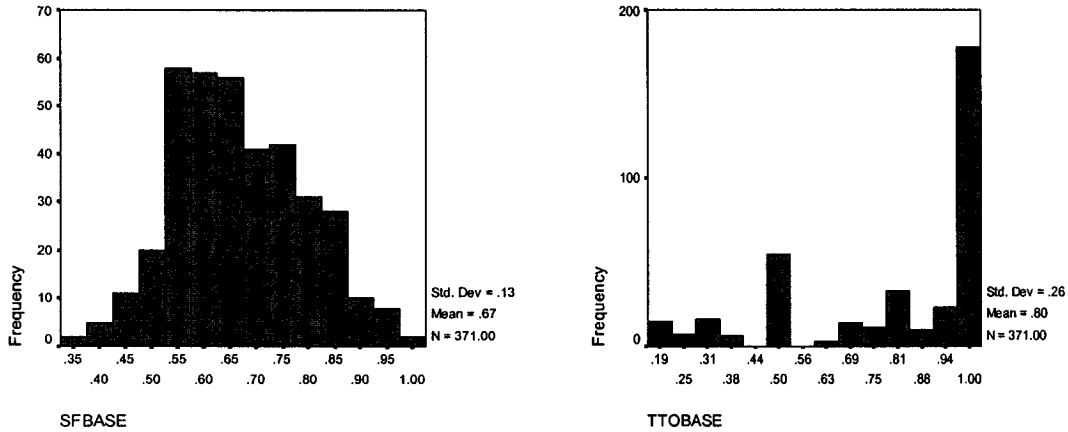
A total of 371 patients completed TTO and SF-6D measures at the baseline evaluation. The mean age of respondents was 57.9 years (+/-10.9), 84.1% were male, with an average of 14.7 years (+/-4.2) of formal education. The referring medical diagnosis of the sample population was coronary bypass graft (45%), angioplasty (32%), myocardial infarction (17%), and angina pectoris (6%).

The mean baseline utility score for the TTO and SF-6D was 0.80 and 0.67 respectively (See Table 1). A difference of -.129 (LCI -.1545 - UCI .1026, $p<0.001$) was observed between measures. Mean scores ranged from 0.666 to 0.766 for the SF-6D and 0.794 to 0.899 for the TTO. Significant differences ($p<0.001$) were observed across all time points. The distribution of utility scores is presented in Figure 1. The TTO was found to display bi-modal distribution of scores that is skewed towards the upper end of the utility scale. The distribution of SF-6D displayed a more distribution of score. The range of baseline scores was 0.17 to 1.0 for the TTO and 0.38 to 1.0 for the SF-6D. Interestingly, 47.9% of baseline utility scores derived from the TTO were at the maximum value of 1 (perfect health) as compared to 5.3% of scores derived from the SF-36 indicating a ceiling effect with the TTO.

Table 4.1: Mean, standard deviation, and 95% confidence intervals for TTO and SF-6D utilities across time-points and QALYs calculated using the area under the curve method.

Time Point	N	Mean TTO	Mean SF-6D	Delta (95% CI)	P Value
Baseline	371	.7940	.6655	-.129 (LCI -.1545 - UCI .1026)	<0.001
3-Months	314	.8725	.7559	-.117 (LCI -.140 – UCI -.0932)	<0.001
6-Months	269	.8815	.7666	- .1149 (LCI -.1384 –UCI -.0915)	<0.001
12-Months	287	.8886	.7621	- .127 (LCI -.1494 – UCI -.1036)	<0.001
15-Months	269	.8991	.7505	- .149 (LCI -.1709– UCI -.1263)	<0.001
24-Months	270	.8482	.7520	- .096 (LCI -.1220– UCI -.0700)	<0.001

Figure 4.1: Comparison of the distribution of SF-6D and TTO utility scores at baseline (N=371)



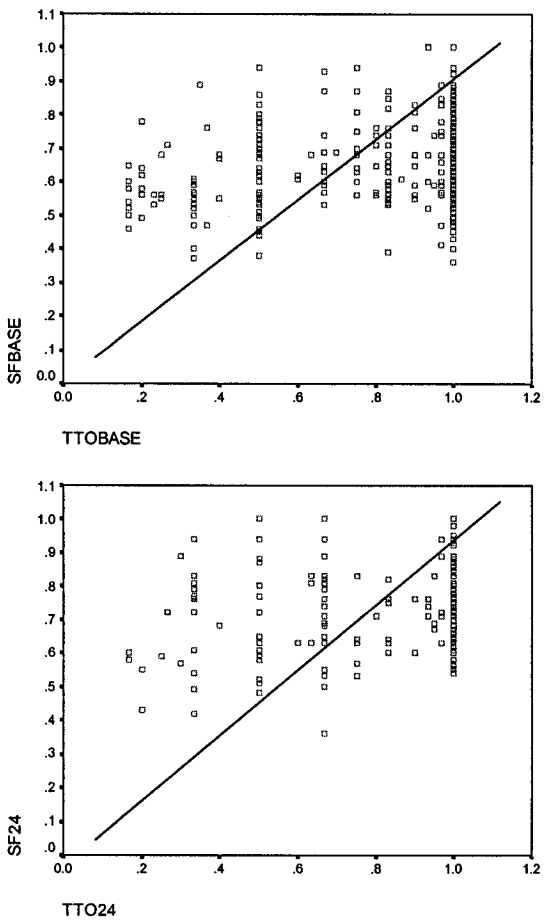
A summary of the correlation coefficients calculated across time-points is displayed in Table 2. Correlations between the instruments ranged between 0.323 at baseline and 0.549 at 24-months ($p<0.001$). A scatter plot of TTO scores against SF-6D scores at baseline and 24-months is presented in Figure 2. Data were found not to cluster tightly around the 45-degree line of perfect agreement. This figure is effective in displaying the range of SF-6D utility scores produced for patients scoring 1.0 on the TTO measure.

Table 4.2: Correlation coefficients for TTO and SF-6D utility scores

Time Point	N	Pearson	Kendall's Tau
Baseline	**371**	**.323****	**.252****
3-Month	**314**	**.389****	**.312****
6-Month	**269**	**.501****	**.311****
12-Month	**287**	**.517****	**.288****
15-Month	**269**	**.576****	**.276****
24-Month	**270**	**.549****	**.307****

**Correlation is significant at the 0.01 level (2-tailed)

Figure 4.2: Scatter plot of baseline and 24-month SF-6D and TTO derived utility scores with 45-degree (perfect agreement) line



The mean utility scores and 2-year QALY for the standard and distributed treatment groups across time is displayed in Table 3 using the TTO and SF-6D methodologies. The mean QALY gain between groups was 0.175 and 0.022 as derived from the SF-6D and TTO. The resulting cost-utility ratio derived for both the TTO and SF-6D is presented in Table 4. A cost-utility ratio of $7,326/QALY gained was calculated based on the SF-6D as compared to a ratio of $5,950/QALY using the TTO utility measure.

Table 4.3: Mean SF-6D Scores for the 3-month, 12-month, and differences between intervention groups over the two-year follow-up period

	SF-6D			TTO		
Time Point	Standard (a)	Distributed (b)	Difference (b-a)	Standard (a)	Distributed (b)	Difference (b-a)
Baseline	0.6805	0.6511	-0.0294	.8035	.7882	-0.0153
3-months	0.7716	0.7390	-0.0326	.8813	.8685	--0.0128
6-months	0.7794	0.7640	-0.0154	.8865	.8901	0.0036
12-months	0.7707	0.7708	0.0001	.8972	.9056	0.0084
15-months	0.7725	0.7568	-0.0157	.9214	.9107	-0.0107
24-months	0.7811	0.7553	-0.0258	.9089	.8201	-0.0888
QALY (2-year)	0.7692	0.75166	-.0175	.8976	.8760	-0.0216

Table 4.4: Estimates of incremental Costs (CDN 2002), Quality Adjusted Life Years (QALYs), and Cost/QALY gained with the 12-month cardiac rehabilitation group at 2-year using differences in the SF-6D utility index

Parameter	SF-6D	TTO
Net HC Expenditures	$ 128.53	$ 128.53
Delta QALY (2-year)	0.017	0.022
Cost / QALY	-$ 7,326	$5,950

4.4 DISCUSSION

Cost-utility analyses are increasingly being used to assess between competing health care interventions. Accurate assessment and interpretation of QALYs is critical to the validity of cost-utility analyses. While a variety of measures exist for calculating utility scores, few studies have conducted direct comparisons between utility scores derived from available scoring systems. This study marks the first evaluation of the new SF-6D preference based health state classification system against the time-trade off direct utility measure. To the best of our knowledge this is also the first application of the SF-6D in a cardiac rehabilitation population.

Utility scores derived from the SF-6D index displayed a larger distribution, while the TTO displayed a clustering of scores at the lower and upper end of the scale. In contrast to previous evaluations, which have found SF-6D to be higher than those from other multi-attribute systems, the SF-6D was found to systematically produce lower scores than the TTO[91]. This study supports the ability of the SF-6D to discriminate against small changes in the upper rage of the utility scale. The TTO and SF-6D were found to produce comparable mean QALY gains over the 2-year assessment period. While differences in the relative cost-utility ratio were observed they were not statistically significant ($7,326/QALY, vs. $5,950/QALY).

Current gold standard direct cost-utility measures such as the TTO are challenging to administer and subject to responder bias. The sensitivity of these tools to the quality of life changes gained from targeted interventions such as cardiac rehabilitation appears to be limited. A ceiling effect was observed with the TTO utility measure. Forty-eight (47.9) percent of respondent's reported a TTO score of 1.0 at baseline representing perfect health. To produce a score of 1.0 respondents have stated a preference for living the remainder of their age predicted life expectancy in their current health state instead of "trading" one or more years of life to be in perfect health. This suggests that close to half of the patient sample would not benefit in terms of QALYs from the intervention.

Cardiac rehabilitation patients tend to be in relatively good health states as compared to other diseased populations. The majority of cardiac rehabilitation patients included in our sample have undergone some form of revascularization procedure (e.g. bypass surgery, angioplasty), which has improved cardiac symptomology. The large size of the SF-6D descriptive system appears to more effectively discriminate between good health states [90] and therefore well suited to the measurement of effectiveness likely to be observed in cardiac rehabilitation populations. There is also an obvious benefit in using a widely accepted health related quality of life (HRQL) tools such as the SF-36 survey for the derivation of utility scores. This tool is currently employed and familiar to many clinicians and researchers in the field of cardiology. Studies have found the SF-36 to be more sensitive than the EQ-5D in detecting changes in HRQL[93].

This study is limited to the evaluation of cardiac rehabilitation patients; the generalizability of these findings is unclear. This study is also limited to comparisons amongst a relatively limited number of health states such as that seen in a cardiac rehabilitation population. Additional investigation will be required to assess the comparability of the SF-6D and TTO across a broader range of health states including those at the lower end of the utility scale.

In conclusion, the SF-6D may be well suited to the assessment of HRQL in cardiac populations given its ability to discriminate among small difference at the upper end of the utility scale. The selection of utility measures should consider the intervention and patient population being evaluated and opportunity for comparisons with other evaluations. Further investigation is required comparing the SF-6D to gold standard measures and within cardiac populations before it can be recommended as the preferred measure.

Appendix 1: Data Extraction Form

Author: _____

Year: _____

Title: _____

Journal: _____

Study Aim	
Perspective	Societal Patient ____ Health Care System ____ Patient ____ Other: _____
Economic Evaluation	Cost Determination ____ Cost Effectiveness ____ Cost Benefit ____ Cost Utility ____ Other: _____
Study Design	Description: RCT: Y / N Incremental Analysis: Y / N
Study Population	
Sample Size	
Comparison Groups	
Intervention Description	
Length of Follow-up	
Primary Outcome Measure(s)	
Outcome Collection Measure(s)	**Societal:** Lost productivity _____ **Patient:** Lost wages _____ Travel costs _____ Time costs _____ **Health Care:** Accommodation _____ Capital Costs _____ Overhead _____ Professional Staff Time _____ Administrative Time _____ Tests and procedures _____ **Other:** _____
Results	Program Cost: _____ Cost per QALY: _____ Cost per YLS: _____ Other: _____
Sensitivity Analysis	
Conclusions	

Appendix 2: Summary of Study Characteristics

Patient Population

Patient Group	# Specific to Group	% of Total	# Including Group	% of Total
Myocardial Infarction (MI)	10	58.8	15	93.8
Coronary Artery Bypass Graft (CABG)	0	0.0	5	31.3
Angioplasty (PTCA)	1	5.9	6	37.5
Combined	4	23.5	4	25.0
Heart Failure	1	5.9	1	5.9
CVD	1	5.9	17	100.0

Analysis Type

Analysis	# of Trials	% of Total
Cost Description	1	5.9
Cost / Utilization Analysis	11	64.7
Cost-Minimization	1	5.9
Cost-Effectiveness	4	23.5
Cost-Utility	1	5.9

Study Design

Design	Overall	% of Total
Randomized Control Trial (RCT)	8	47.8
Non-Randomized	4	23.5
Modeling	4	23.5
Cohort Study	1	5.9

Perspective

Perspective	Overall	% of Total
Societal	5	29.4
Health Care System	9	52.9
Rehabilitation Program	3	17.6
Patients	4	23.5

Appendix 3: Summary of Comparative Studies

Supervised CR vs. Standard Care

Author	Perspective	Analysis	Estimate of Cost, C/E, C/U
Georgiou (2001)	Limited Societal	Modeling cost-effectiveness	$1,773 USD/ LYS
Lowensteyn (2000)	Societal	Modeling cost-effectiveness	Less than $15,000 USD/ LYS
Ades (1997)	Payee of health care expenses	Modeling cost-effectiveness	$4,950 USD/ LYS
Oldridge (1993)	Societal	Cost-effectiveness Cost-utility	$21,800 USD / LYG $9,200 USD/QALY (1-year follow-up)
Ades (1992)	Hospital	Cost analysis	Per capita hospitalization $739 less in CR group (21-months follow-up)
Levin (1991)	Societal	Cost analysis	Per patient cost SEK 73,5000 ($11,500 USD) lower in CR group (over 5-years)

Home-Based CR vs. Standard Care

Author	Perspective	Analysis	Estimate of Cost, C/E, C/U, Other
Robertson (2001)	In-patient health care system	Cost effectiveness	Incremental cost savings of $17,216 CND favoring home program
Lowensteyn (2000)	Societal	Modeling cost effectiveness	Less than $12,000 USD/ LYS
Bondestam (1995)	Payee of health care expenses	Utilization analysis	Mean number re-hospitalizations 2.1 for intervention group and 5.4 for control group

Supervised CR vs. Home-Based CR

Author	Perspective	Analysis	Estimate of Cost, C/E
Collins (2001)	Rehabilitation program and patients	Modeling cost analysis	Incremental savings of $405 with home-based program
Lowensteyn (2000)	Societal	Modeling cost-effectiveness	Incremental C/E of home program is $3000/LYS
DeBusk (1985)	Rehabilitation program	Cost-minimization	Home program produced incremental savings of $392 per patient

Delivery Models / Components

Author	Perspective	Analysis	Intervention	Estimate of Costs
Carlson (2000)	Rehabilitation program	Cost analysis	CR vs. CR for 4-weeks then weaned to home-based	Incremental savings $738 USD with modified protocol
Nieuwland (2000)	Rehabilitation program	Cost analysis	High frequency CR vs. Low frequency CR	Incremental savings $2182 Euro
Dixhoorn (1999)	Health care system (cardiac)	Utilization analysis	Exercise + Relaxation vs. Relaxation alone	Readmission frequency reduced by 30% with relaxation the therapy (0.98 control vs. 0.68)
Edwards (1993)	Health Care system (cardiac)	Cost analysis	Exercise + Counseling vs. Counseling only	No significant differences btw groups Cost savings of $2597 in exercise + counseling group

Appendix 4: Drummond Reviews

Drummond Review - Collins (2001)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		While there was no single comprehensive statement describing perspective and comparators, the authors were explicit in identifying this information.
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Program delivery costs were estimated prospectively and re-hospitalization rates were modeled from published RCT data.
1.2 Did the study involve a comparison of alternatives?	X			Gym-based and home-based cardiac rehabilitation programs were compared
1.3 Was a viewpoint for the analysis stated and was the study places in any particular decision making context?	X			The authors state the analysis is conducted from the viewpoint of program funders and patients. The analysis appears to take the perspective of the health care system as well.
2. Was a comprehensive description of competing alternatives given?	X			A detailed description of the interventions being compared was provided.
2.1 Were any important alternatives omitted?	X			Standard care was not assessed.
2.2 Was (should) a do nothing alternative (be) considered?		X		No standard care alternative was considered.
3. Was there evidence that the programmes' effectiveness had been established?		X		The evidence of effectiveness between the gym and home-based programs was inadequate.
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Hospital readmission rates were derived from the Westcop trial, an Australian database of 94 MI and/or angina patients followed for 18-months. Differences in re-admission rates were extrapolated for CR and non-CR participants and applied to both comparison groups.
4. Where all the important and relevant costs and consequences for each alternative identified?	X			The costs and consequences identified were adequate.
4.1 Was the range wide enough for the research question at hand?	X			
4.2 Did it cover all relevant viewpoints?	X			The societal perspective was partially evaluated and is less important.
4.3 Were capital costs, as well as operating costs, included?	X			All important program delivery costs were evaluated.
5. Were costs and consequences measured accurately in appropriate physical units?	X			The quantification of consequences was inadequate for the conclusions drawn.
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		No prospective collection of cost or re-hospitalization data was conducted. Re-hospitalization rates were extrapolated from the Westcop trial and assumed to be equivalent for both gym-based and home-based programs and there for carried no weight. There is no evidence to support the application of this assumption.
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?		-		
6. Were costs and consequences valued credibly?		X		The assumptions applied in this modeling exercise were inadequate.
6.1 Were the sources of all values clearly identified?	X			Sources for costs and consequences were adequately described.
6.2 Were market values employed for changes involving resources gained or depleted?		X		Hospital databases and records were utilized with supplements form market values (charges) where necessary.
6.3 Where market values were absent (e.g volunteer labour), or market did not reflect actual values?		-		N/A
6.4 Was the valuation of consequences appropriate for the question posed?		X		The use of the Westcop database for re-hospitalization rates was inadequate given the small sample size, no differentiation between home and gym based programs, and the data was collected in a different country.
7. Were the costs and consequences adjusted for differential timing?		X		The authors state the lack of discounting in this exercise as a limitation given costs and consequences collected over a 3-year period from a variety of sources and not were adjusted for differential timing.
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		Equipment was discounted at a rate of 27%. No other description of discounting is provided.
7.2 Was any justification given for the discount rate used?	X			The authors reference the Australian taxation office and Drummond 1997 for discount rate applied to the equipment.
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			An incremental cost savings of $405 was reported for the home-based program.
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		The study resulted in a cost-minimization analysis.
9. Was a sensitivity analysis performed?	X			7-variables were utilized in the sensitivity analysis
9.1 Was justification provided for the ranges of values (for key study parameters) employed in the sensitivity analysis?		X		No explanation of ranges was provided.
9.2 Were study results sensitive to changes in the values (within the assumed range)?		X		The home-based program was consistently found to be the least cost alternative for most sensitivity ranges.
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences?		X		A cost minimization analysis was conducted in which incremental delivery costs was reported.
10.2 Were the results compared with those of others who have investigated the same question?		X		The authors report that to date no trials have conducted a cost-analysis of gym based and home based programs. No comparisons are made with the findings of other economic evaluations of CR.
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The authors suggest the findings are likely to be generalizable.
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The number of patients reached, increased patient compliance, and satisfaction was identified by the authors as a benefit of the home-program.
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	X			The authors discuss the potential for expanding the reach of CR services using a home-based delivery model in rural and other populations.

Drummond Review - Robertson (2001)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		The research question does not clearly state the comparison groups.
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Program delivery costs and in-patient re-hospitaliztaion were considered.
1.2 Did the study involve a comparison of alternatives?	X			A home-based program was compared to usual care.
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No perspective is tested by the authors but the perspective appears to be that of the health care system limited to re-hospitalizations.
2. Was a comprehensive description of competing alternatives given?	X			An adequate description was provided.
2.1 Were any important alternatives omitted?		X		The alternatives were adequate for the early post MI period under evaluation.
2.2 Was (should) a do nothing alternative (be) considered?	X			A do nothing alternative was considered via the usual care group.
3. Was there evidence that the programmes' effectiveness had been established?		X		
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		The study was conducted using a RCT design, however the sample size was inadequate for evaluation of clinical effectiveness.
4. Were all the important and relevant costs and consequences for each alternative identified?		X		Limited program delivery and re-hospitalization admissions were considered.
4.1 Was the range wide enough for the research question at hand?		X		Only in-patient re-hospitalizations and staff time were considered.
4.2 Did it cover all relevant viewpoints?		X		Only a limited partial evaluation of in-patient and program delivery health care costs were considered.
4.3 Were capital costs, as well as operating costs, included?			N/A	Capital costs were not included for the home based program.
5. Were costs and consequences measured accurately in appropriate physical units?		X		Nursing staff time was estimated rather than logged per patient. Mean re-hospitalization rates were compared for patient groups.
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	X			Program delivery costs were estimated not measured directly per patient. 6-month re-hospitalizations were collected but not reported or considered in the analysis. The author's explanation for not reporting 6-mont data raises questions.
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	X			The control group was assumed to have zero costs to the in-patient system; it is difficult to determine if inpatient nursing time was increased with control group patients.
6. Were costs and consequences valued credibly?		X		A standard hospitalization rate was applied for all patients regardless of DRG. Nursing staff time appears to be valued credibly but do not reflect national or international averages.
6.1 Were the sources of all values clearly identified?		X		No source for the re-hospitalization rate applied is offered.
6.2 Were market values employed for changes involving resources gained or depleted?			X	The authors are unclear if wages and re-hospitalizations are standardized.
6.3 Where market values were absent were adjustments made to approximate market values?			X	The authors do not report basis for values provided.
6.4 Was the valuation of consequences appropriate for the question posed?			X	The use of a mean hospital charge is questionable.
7. Were the costs and consequences adjusted for differential timing?				N/A; All costs were collected over a 6-week period.
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?				N/A
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			The control group was assumed to have zero costs to the in-patient system.
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	X			
9. Was a sensitivity analysis performed?		X		No analysis was conducted
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		No comparison to other studies was conducted.
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	X			A cost / consequences ratio was reported.
10.2 Were the results compared with those of others who have investigated the same question?		X		The authors did not compare their findings with that reported in the literature.
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The authors caution that the small sample size, and inclusion of only first time MI patients limits the generalizability of this study.
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The study discussed the difficulty in-patient nurses have in providing education and counseling to patients in the early post MI period and the utility of a structured outpatient intervention.
10.5 Did the study discuss issues of implementation?	X			See 10.4

Drummond Review - Georgiou (2000)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		The authors statement of purpose lacks a statement of perspective and of comparators
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?	X			Cost and consequences were reported
1.2 Did the study involve a comparison of alternatives?	X			Standard care and exercise based CR were compared
1.3 Was a viewpoint for the analysis stated and was the study places in any particular decision making context?		X		No clear statement of perspective was made, however the authors indicate the costs included in the analysis with the introductory paragraphs
2. Was a comprehensive description of competing alternatives given?	X			A comprehensive description of the intervention group was provided
2.1 Were any important alternatives omitted?		X		Standard care was the comparator of primary importance
2.2 Was (should) a do nothing alternative (be) considered?	X			A standard care comparator was utilized
3. Was there evidence that the programmes' effectiveness had been established?	X			Randomized control trial evidence supported improved survival within intervention group
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			The study was conducted alongside the largest randomized control trial to evaluate the effects of CR in a heart failure population [63]
4. Where all the important and relevant costs and consequences for each alternative identified?	X			The author identified the main costs attributed to a societal perspective, but did not include indirect or travel costs accrued by the patient.
4.1 Was the range wide enough for the research question at hand?	X			The range selected was adequate for the analysis.
4.2 Did it cover all relevant viewpoints?		X		The study utilized a limited societal perspective. Not included in the analysis was the cost of travel to participate in the exercise sessions.
4.3 Were capital costs, as well as operating costs, included?	X			Equipment and rented space were included in the direct cost estimate
5. Were costs and consequences measured accurately in appropriate physical units?		X		In this modeling study estimates for all costs components were utilized. No direct measurement was conducted along side the RCT.
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		None
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?		X		None
6. Were costs and consequences valued credibly?	X			Estimates form several sources were combined to form the estimate of costs and consequences within this modeling study
6.1 Were the sources of all values clearly identified?	X			Adequately identified
6.2 Were market values employed for changes involving resources gained or depleted?	X			Market values used to calculate wages lost
6.3 Where market values were absent (e.g volunteer labour), or market did not reflect actual values?				N/A
6.4 Was the valuation of consequences appropriate for the question posed?	X			Based on RCT data
7. Were the costs and consequences adjusted for differential timing?	X			A discount rate of 3% was applied to costs and consequences
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?	X			
7.2 Was any justification given for the discount rate used?	X			Standard US discount rate
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			A cost-effectiveness analysis was conducted comparing incremental differences between groups
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	X			
9. Was a sensitivity analysis performed?	X			Sensitivity analysis performed
9.1 Was justification provided for the ranges of values (for key study parameters) employed in the sensitivity analysis?	X			Provided within the results section
9.2 Were study results sensitive to changes in the values (within the assumed range)?		X		The intervention group remained a cost effective alternative
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		The discussion section focused only on the limitations of the study and reasons for possible underestimation and did not place the findings into a broader context.
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences?	X			Cost/LYS
10.2 Were the results compared with those of others who have investigated the same question?		X		This is the first C/E analysis in a heart failure sample. The author did not compare findings to that seen in other CVD populations.
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The authors note the study generalizability is limited through the inclusion of only NYHF Class II-III patients
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?		X		No discussion provided on this topic
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?		X		No discussion provided on this topic

Drummond Review *- Lowenstyn (2000)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		An explicit statement of the analysis perspective is not provided.
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?	X			Costs/YOLS were assessed.
1.2 Did the study involve a comparison of alternatives?	X			Supervised and unsupervised program were compared.
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No viewpoint was explicitly stated but the perspective appears to be **societal**
2. Was a comprehensive description of competing alternatives given?	X			An adequate description of competing interventions was provided.
2.1 Were any important alternatives omitted?	X			Standard care.
2.2 Was (should) a do nothing alternative (be) considered?	X			A standard care alternative could have been considered.
3. Was there evidence that the programmes' effectiveness had been established?		X		A simulation model was used to estimate program effectiveness based on published effectiveness data of exercise on CVD risk factors
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Validated disease simulation model was utilized. The use of a model presents limitations upon the study findings.
4. Were all the important and relevant costs and consequences for each alternative identified?	X			The costs and consequences identified ere adequate.
4.1 Was the range wide enough for the research question at hand?	X			The range was sufficient to answer the question posed
4.2 Did it cover all relevant viewpoints?	X			A societal perspective applies a comprehensive evaluation.
4.3 Were capital costs, as well as operating costs, included?			X	No breakdown of costs is provided for supervised program delivery cost estimates
5. Were costs and consequences measured accurately in appropriate physical units?		X		Estimates were utilized for costs with no direct measurement
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	X			Health care use was not assessed.
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	Unable to assess.
6. Were costs and consequences valued credibly?		X		The valuation of program delivery costs was estimated and may be inadequate.
6.1 Were the sources of all values clearly identified?		X		The sources of estimates provided for supervised and unsupervised programs. Health care cost sources are well described.
6.2 Were market values employed for changes involving resources gained or depleted?	X			Health care insurance fees were utilized.
6.3 Where market values were absent were adjustments made to approximate market values?			X	There is no clear identification of estimates for program delivery costs
6.4 Was the valuation of consequences appropriate for the question posed?		X		A prospective measurement of costs would have strengthened the present analysis
7. Were the costs and consequences adjusted for differential timing?	X			A 3% discount rate was applied and discount was evaluated within the sensitivity analysis
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?				See above
7.2 Was any justification given for the discount rate used?	X			Standard rate.
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			The analysis was incremental.
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	X			Cost/YOLS
9. Was a sensitivity analysis performed?	X			3 variables were included in the sensitivity analysis
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?		X		No justification was provided for the sensitivity analysis employed.
9.2 Were study results sensitive to changes in the values?	X			The analysis was sensitive to changes in values
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			An adequate discussion of results was provided.
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	X			A cost-effectiveness ratio was reported.
10.2 Were the results compared with those of others who have investigated the same question?	X			A limited comparison to other CDV interventions was conducted but CR cost effectiveness studies.
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		The study appears to advocate the generalizability of the study, no limitations are recognized.
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Compliance with intervention was discussed as a factor likely to influence cost effectiveness.
10.5 Did the study discuss issues of implementation?		X		Few issues regarding implementation are addressed.

Drummond Review - Carlson (2000)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		No comprehensive statement of comparators, perspective, and outcome measures
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		This study included only a description of costs
1.2 Did the study involve a comparison of alternatives?	X			Comparison of a home based and supervised exercise program
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		Within the methods the authors describe
2. Was a comprehensive description of competing alternatives given?	X			A comprehensive description with diagram was provided
2.1 Were any important alternatives omitted?	X			Standard care.
2.2 Was (should) a do nothing alternative (be) considered?		X		Standard care would be a valuable comparator
3. Was there evidence that the programmes' effectiveness had been established?	X			RCT evidence supports effectiveness
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			RCT
4. Were all the important and relevant costs and consequences for each alternative identified?		X		A limited cost horizon was evaluated and consequences were not included in the analysis
4.1 Was the range wide enough for the research question at hand?		X		Staff time, treadmill, and blood tests were the only costs considered.
4.2 Did it cover all relevant viewpoints?		X		A quasi-perspective was utilized in the analysis. The health care system was not considered and should have been included.
4.3 Were capital costs, as well as operating costs, included?		X		Capital and operating costs were not identified for inclusion
5. Were costs and consequences measured accurately in appropriate physical units?		X		Means were utilized for valuation of comparison group resources
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		All items identified were presented in the analysis
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	None identified
6. Were costs and consequences valued credibly?			X	No description of valuation sources utilized was provided
6.1 Were the sources of all values clearly identified?		X		No identification of sources was provided
6.2 Were market values employed for changes involving resources gained or depleted?			X	Not enough information to assess
6.3 Where market values were absent were adjustments made to approximate market values?			X	Not enough information to assess
6.4 Was the valuation of consequences appropriate for the question posed?		X		Consequences were not considered and limit this analysis
7. Were the costs and consequences adjusted for differential timing?		X		No period was specified for the collection of data and no evidence of discounting was found.
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?				N/A
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		A per patient cost was provided for both alternatives but no incremental comparison was provided.
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		Means were compared for the cost measures included in the analysis.
9. Was a sensitivity analysis performed?		X		No sensitivity analysis was performed.
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		The discussion of the cost analysis findings was limited and inadequate.
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio was utilized.
10.2 Were the results compared with those of others who have investigated the same question?		X		No comparison with other cost-descriptions or effectiveness studies was offered.
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		The authors emphasize the findings are relevant to low to moderate risk cardiac patients and programs which emphasize independent exercise.
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The home program was found to improve adherence rates and may positively impact on long-term adherence. In addition a home based provides a population health approach.
10.5 Did the study discuss issues of implementation?	X			The authors suggest a focus be placed on a methodological approach that emphasizes independent exercise.

Drummond Review *- Nieuwland (2000)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		No explicit statement regarding perspective and limited to identification of program delivery costs
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Program delivery costs were identified.
1.2 Did the study involve a comparison of alternatives?	X			High frequency and low frequency CR programs were compared
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		Not explicitly stated.
2. Was a comprehensive description of competing alternatives given?	X			An adequate description of costs was provided
2.1 Were any important alternatives omitted?	X			Standard care
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care comparison group
3. Was there evidence that the programmes' effectiveness had been established?	X			Via RCT
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			Effectiveness evaluated via RCT
4. Were all the important and relevant costs and consequences for each alternative identified?		X		There were several weakness noted
4.1 Was the range wide enough for the research question at hand?		X		The range did not include all relevant costs
4.2 Did it cover all relevant viewpoints?		X		The societal, health care, and patient viewpoints were not considered
4.3 Were capital costs, as well as operating costs, included?			X	No description of cumulative cost estimates is provided
5. Were costs and consequences measured accurately in appropriate physical units?			X	We are unable to assess the methods utilized for cost estimates
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?			X	Unable to assess
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	Unable to assess
6. Were costs and consequences valued credibly?		X		We are unable to judge he credibility of resource valuation based on the information provided. No consequence is referenced
6.1 Were the sources of all values clearly identified?		X		Sources are not clearly identified
6.2 Were market values employed for changes involving resources gained or depleted?			X	No description of costing sources is provided
6.3 Where market values were absent were adjustments made to approximate market values?				N/A
6.4 Was the valuation of consequences appropriate for the question posed?		X		No valuation of consequences was conducted
7. Were the costs and consequences adjusted for differential timing?				N/A
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?				N/A
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		No incremental analysis conducted
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		No comparison of incremental costs and consequences
9. Was a sensitivity analysis performed?		X		None conducted
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?		X		-
9.2 Were study results sensitive to changes in the values?		X		-
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		The authors do not reference costs in their discussion
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio or index was provided.
10.2 Were the results compared with those of others who have investigated the same question?		X		No discussion of global cost findings was provided
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The authors identify the limitations of the study sample utilized
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The feasibility and adherence to high intensity programs was discussed by authors as a limiting factor
10.5 Did the study discuss issues of implementation?		X		No discussion relevant to the economic evaluation

Drummond Review – DixHoorn (1999)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		No clear statement was provided describing comparison groups and perspective. The authors suggest cost effectiveness is being studied
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Program delivery costs were not evaluated. The primary outcome measure was re-hospitalization rate.
1.2 Did the study involve a comparison of alternatives?	X			Relaxation therapy + exercise or exercise only
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No viewpoint was stated, a limited health care perspective has been utilized.
2. Was a comprehensive description of competing alternatives given?	X			Interventions were well described
2.1 Were any important alternatives omitted?	X			Standard care, therapy only
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care group
3. Was there evidence that the programmes' effectiveness had been established?	X			Via RCT
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			Via RCT
4. Were all the important and relevant costs and consequences for each alternative identified?		X		The program delivery costs should have been considered
4.1 Was the range wide enough for the research question at hand?		X		Program delivery costs were not considered
4.2 Did it cover all relevant viewpoints?		X		The rehabilitation program, patient, and societal perspectives were omitted
4.3 Were capital costs, as well as operating costs, included?		X		No costs were evaluated
5. Were costs and consequences measured accurately in appropriate physical units?		X		No program delivery costs measured.
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		
5.2 Were there any special circumstances that made measurement difficult? Were these circumstances handled appropriately?		X		
6. Were costs and consequences valued credibly?				Program delivery costs and re-hospitalizations were not valued
6.1 Were the sources of all values clearly identified?				N/A
6.2 Were market values employed for changes involving resources gained or depleted?				N/A
6.3 Where market values were absent were adjustments made to approximate market values?				N/A
6.4 Was the valuation of consequences appropriate for the question posed?		X		A cost-effectiveness analysis would have added to the value of the studies findings
7. Were the costs and consequences adjusted for differential timing?		X		No value was placed on costs
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?				-
7.2 Was any justification given for the discount rate used?				-
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		Costs were not assessed
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		See above
9. Was a sensitivity analysis performed?		X		No sensitivity analysis conducted
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		A limited discussion was provided
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs consequences?		X		Simple unit measures provided
10.2 Were the results compared with those of others who have investigated the same question?		X		No comparison made of findings to existing literature
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		Little discussion provided
10.4 Did the study take account of, other important factors in the choice or decision under consideration?	X			Confounding influence of depressed patients within sample
10.5 Did the study discuss issues of implementation, such as the feasibility?	X			The quality of relaxation theory provided was identified as an important confounder

Drummond Review – Ades (1997)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?	X			**Good question stated**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?	X			Cost / YLS
1.2 Did the study involve a comparison of alternatives?	X			Supervised CR was compared to standard care
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?	X			Hospital / Health acre system
2. Was a comprehensive description of competing alternatives given?	X			Adequate description provided for standard CRP
2.1 Were any important alternatives omitted?		X		None
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care was included
3. Was there evidence that the programmes' effectiveness had been established?	X			Previously established, no new effectiveness information provided
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Previous RCT – present study modeled C?E
4. Were all the important and relevant costs and consequences for each alternative identified?	X			An adequate analytical perspective was utilized
4.1 Was the range wide enough for the research question at hand?	X			The rehabilitation program costs generated from survey of programs
4.2 Did it cover all relevant viewpoints?		X		The patient, larger societal perspective was not considered in the derivation of costs
4.3 Were capital costs, as well as operating costs, included?			X	Unable to assess
5. Were costs and consequences measured accurately in appropriate physical units?	X			Use of cost effectiveness analysis means both cost and consequences were considered
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	X			None presented
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	None present in publication
6. Were costs and consequences valued credibly?			X	Sources were not clearly identified – were derived from survey of existing programs
6.1 Were the sources of all values clearly identified?			X	See above
6.2 Were market values employed for changes involving resources gained or depleted?			X	See above
6.3 Where market values were absent were adjustments made to approximate market values?			X	See above
6.4 Was the valuation of consequences appropriate for the question posed?	X			Cost-effectiveness analysis appropriate
7. Were the costs and consequences adjusted for differential timing?	X			Cost were discounted at 5% to reflect 1995 values
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?	X			Consequences were not discounted
7.2 Was any justification given for the discount rate used?	X			No specific statement
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			Incremental $ / YLS ratio provided
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	X			See above
9. Was a sensitivity analysis performed?	X			A sensitivity analysis based on 3-variables was conducted
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?		X		The description of ranges employed within the sensitivity analysis was adequate
9.2 Were study results sensitive to changes in the values?	X			The sensitivity analysis varied results between $0/YLS and $20,000/YLS
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			Discussion was adequate
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	X			$ / YLS
10.2 Were the results compared with those of others who have investigated the same question?	X			Adequate comparisons made
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			Sample was mostly male limiting the generalizability to female cardiac patients
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?		X		Little discussion
10.5 Did the study discuss issues of implementation?		X		Little discussion

Drummond Review – Bondestam (1995)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		A limited perspective and analysis was posed.
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		The study was limited to the evaluation of re-hospitalizations.
1.2 Did the study involve a comparison of alternatives?	X			Rehabilitation and control group compared
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?	X			The authors state the study is limited to the utilization of resources outside the program
2. Was a comprehensive description of competing alternatives given?	X			A comprehensive description of the rehabilitation program was provided
2.1 Were any important alternatives omitted?		X		
2.2 Was (should) a do nothing alternative (be) considered?	X			A control group was utilized
3. Was there evidence that the programmes' effectiveness had been established?		X		Non-randomized study comparing matched patients from two health districts
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		There was. The level of evidence is weak given the non-randomized design and differences detected In age and sex between comparison groups.
4. Were all the important and relevant costs and consequences for each alternative identified?		X		A severely limited analytical perspective and cost horizon was reported by investigators. The study neglects to include non-hospital consequences and program delivery costs
4.1 Was the range wide enough for the research question at hand?		X		Program delivery costs were not reported
4.2 Did it cover all relevant viewpoints?		X		The viewpoint was limited to the health care provider (health care system), societal, patient, and rehabilitation program costs were not assessed.
4.3 Were capital costs, as well as operating costs, included?		X		No program delivery costs were reported
5. Were costs and consequences measured accurately in appropriate physical units?		X		Costs were not measured. Re-hospitalizations were reported as the number for admission and length of stay which is appropriate.
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?	X			Out-patient medical costs were not reported
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	None reported
6. Were costs and consequences valued credibly?		X		Hospitalization were reported in their natural units no attempt was made to assign financial value
6.1 Were the sources of all values clearly identified?		X		N/A
6.2 Were market values employed for changes involving resources gained or depleted?		X		N/A
6.3 Where market values were absent were adjustments made to approximate market values?		X		N/A
6.4 Was the valuation of consequences appropriate for the question posed?		X		The dollar value of costs and consequences allows for more thorough assessment
7. Were the costs and consequences adjusted for differential timing?		X		Costs were not reported and therefore no discounting was applied
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		N/A
7.2 Was any justification given for the discount rate used?		X		N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		Costs were not evaluated therefore the incremental analysis was lacking
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		None conducted
9. Was a sensitivity analysis performed?		X		No sensitivity analysis was performed
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		The discussion of findings was limited
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No index was provided given costs were not assessed
10.2 Were the results compared with those of others who have investigated the same question?	X			A limited comparison to published research was provided
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		Findings reported as specific to cardiac patients greater than 65 years of age
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Participation in the supervised program was reported to be 21%. Strategies are suggested to improve participation rates.
10.5 Did the study discuss issues of implementation?	X			The authors emphasize the importance of early intervention

Drummond Review – Allison (1995)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		The question is appropriate fro the study design
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Only consequences (re-hospitalizations) were assessed
1.2 Did the study involve a comparison of alternatives?		X		A single intervention was compared with respect to its effects on patient cohorts
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No explicit statement of perspective was provided, however authors indicate re-hospitalizations as their outcome measure
2. Was a comprehensive description of competing alternatives given?	X			An adequate description was provided of the rehabilitation program
2.1 Were any important alternatives omitted?		X		Cohort study design
2.2 Was (should) a do nothing alternative (be) considered?		X		Cohort study design
3. Was there evidence that the programmes' effectiveness had been established?		X		No evidence of effectiveness was provided
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Cohort study design was utilized limiting the level of evidence provided
4. Were all the important and relevant costs and consequences for each alternative identified?		X		Resources consumed by the cohorts were not evaluated
4.1 Was the range wide enough for the research question at hand?	X			
4.2 Did it cover all relevant viewpoints?		X		A societal viewpoint would be appropriate and was not included
4.3 Were capital costs, as well as operating costs, included?		X		No program delivery costs were provided
5. Were costs and consequences measured accurately in appropriate physical units?		X		No DRG was identified
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	Unable to assess
6. Were costs and consequences valued credibly?		X		A mean cost was applied to all hospital admissions
6.1 Were the sources of all values clearly identified?		x		No information regarding source of values applied was provided
6.2 Were market values employed for changes involving resources gained or depleted?			X	Unable to assess
6.3 Where market values were absent were adjustments made to approximate market values?			X	Unable to assess
6.4 Was the valuation of consequences appropriate for the question posed?			X	Unable to assess
7. Were the costs and consequences adjusted for differential timing?		X		No evidence of adjustments for differential timing. No report for data collection of length of data collection period
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		No evidence provided
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		AN incremental re-hospitalization costs were reported
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		Only costs reported
9. Was a sensitivity analysis performed?		X		None reported
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results include all issues of concern to users?		X		Limited discussion was provided. Authors ail to discuss resource consumption of cohorts and program, elements
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio was provided given only consequences were assessed
10.2 Were the results compared with those of others who have investigated the same question?	X			An adequate comparison of other published literature was provided
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The diverse group of patients utilized in the investigation is noted by authors as a strength of the studies findings
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?		X		Many distressed patients may not take part in CR programs
10.5 Did the study discuss issues of implementation?		X		No specific discussion

Drummond Review - Edwards (1993)

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**The perspective is not made clear within the research question**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Hospital readmissions and health care expenditures were considered
1.2 Did the study involve a comparison of alternatives?	X			Exercise and non-exercise rehabilitation was compared
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No explicit statement
2. Was a comprehensive description of competing alternatives given?	X			An adequate description of the interventions was provided
2.1 Were any important alternatives omitted?	X			Standard care
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care comparator would add value
3. Was there evidence that the programmes' effectiveness had been established?		X		The evidence of effectiveness has not been provided by this retrospective analysis of small sample size.
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Retrospective costs analysis – evidence weak
4. Were all the important and relevant costs and consequences for each alternative identified?		X		A broad range of costs and consequences were identified by the authors
4.1 Was the range wide enough for the research question at hand?	X			A broad cost range is proposed
4.2 Did it cover all relevant viewpoints?		X		Patient costs were not evaluated
4.3 Were capital costs, as well as operating costs, included?	X			
5. Were costs and consequences measured accurately in appropriate physical units?			X	The format for including program delivery costs is questionable
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?			X	The measurement of Phase II and III rehabilitation program costs is not well described.
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	Unable to assess
6. Were costs and consequences valued credibly?			X	A limited presentation of costing sources is presented
6.1 Were the sources of all values clearly identified?		X		Sources were not clearly identified
6.2 Were market values employed for changes involving resources gained or depleted?			X	
6.3 Where market values were absent were adjustments made to approximate market values?			X	
6.4 Was the valuation of consequences appropriate for the question posed?			X	
7. Were the costs and consequences adjusted for differential timing?		X		No discounting occurred
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		N/A given 1-year follow-up period
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		No incremental
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		
9. Was a sensitivity analysis performed?		X		None reported
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			Despite the lack of reporting incremental ratios for cost effectiveness this analysis has a strong discussion section
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio provided
10.2 Were the results compared with those of others who have investigated the same question?	X			Adequate comparisons are more with the findings of other investigators
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The study addresses generalizability in its conclusion and suggests the application to other patient groups remains to be determined.
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The authors suggest compliance made be improved by the home based program.
10.5 Did the study discuss issues of implementation?	X			The study suggests further analysis is required to support this retrospective analysis

Drummond Review *- Oldridge (1993)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**The authors do not provide a clear statement of purpose summarizing the study perspective and the alternatives.**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?	X			An examination of both program associated costs and the consequences were assessed.
1.2 Did the study involve a comparison of alternatives?	X			Standard care is compared to an 8-week cardiac rehabilitation intervention.
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No explicit statement regarding the perspective from which this analysis was conducted. The authors state that both program and patient costs were assessed. In addition health care utilization was monitored.
2. Was a comprehensive description of competing alternatives given?		X		The authors provide a description of the 8-week cardiac rehabilitation intervention but fail to include eh frequency of exercise classes and other contacts. No descriptive statement is provided regarding standard care in the region.
2.1 Were any important alternatives omitted?		X		The two groups selected for comparison are adequate for establishing the cost effectiveness/ utility of cardiac rehabilitation program.
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care was included as the comparison group.
3. Was there evidence that the programmes' effectiveness had been established?			X	A previous publication had described findings regarding the programs effectiveness on patient quality of life. The CR group experienced accelerated recovery at 3-month but no differences was found at 12-months.
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			A RCT design was utilized in which utility costs were measured prospectively. Survival data was taken from published meta-analysis findings.
4. Were all the important and relevant costs and consequences for each alternative identified?	X			It is unclear if overhead costs were included in the analysis.
4.1 Was the range wide enough for the research question at hand?	X			The range of costs was wide enough to assess the cost utility of the cardiac rehabilitation program.
4.2 Did it cover all relevant viewpoints?	X			
4.3 Were capital costs, as well as operating costs, included?	X			Capital and operating costs were included in the analysis. It is not clear if overhead has been considered.
5. Were costs and consequences measured accurately in appropriate physical units?	X			Most costs and consequences were measured adequately
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?			X	The authors provide no description of special circumstances.
6. Were costs and consequences valued credibly?			X	
6.1 Were the sources of all values clearly identified?		X		The source of cost values was not identified by the authors.
6.2 Were market values employed for changes involving resources gained or depleted?			X	
6.3 Where market values were absent were adjustments made to approximate market values?			X	Bets estimates were utilized
6.4 Was the valuation of consequences appropriate for the question posed?	X			Cost-utility was assessed using the Time Trade-Off measure; a validated preference based utility index and YLS.
7. Were the costs and consequences adjusted for differential timing?		X		Costs were discounted at 5% and varied as part of the sensitivity analysis
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		See above
7.2 Was any justification given for the discount rate used?		X		Best estimate
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			Data was reported by patient group and incrementally.
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?	X			See above
9. Was a sensitivity analysis performed?	X			A limited sensitivity analysis was performed
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?	X			Sensitivity analysis were conducted around the lower and upper confidence limits of the mean TTO change scores.
9.2 Were study results sensitive to changes in the values?		X		The findings remain robust through the ranges evaluated in the sensitivity analysis
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			An adequate discussion section is provided which addresses generalizability, previous research, and implementation.
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?	X			The authors have addressed possible interpretations of the cost indexes and provided readers with context for data interpretation.
10.2 Were the results compared with those of others who have investigated the same question?	X			The discussion includes minimal comparison to previous CR investigations but includes a detailed comparison with competing cardiac interventions
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			The study sates the generalizability of the study is unclear. A detailed discussion of strengths and weaknesses is provided
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			The study discussed the potential for larger increases in quality of life for medically complex and older patients
10.5 Did the study discuss issues of implementation?	X			The study addressed the importance of intervention soon after MI

Drummond Review - *Ades (1993)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?	X			**Descriptive question provided**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Only costs considered
1.2 Did the study involve a comparison of alternatives?	X			Standard case to usual care
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?	X			Authors state limited to hospital charges
2. Was a comprehensive description of competing alternatives given?	X			Adequate description provided
2.1 Were any important alternatives omitted?		X		None omitted
2.2 Was (should) a do nothing alternative (be) considered?	X			Usual care considered
3. Was there evidence that the programmes' effectiveness had been established?		X		Level of evidence reduced due o non randomized cohort study design
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Non randomized cohort study design
4. Were all the important and relevant costs and consequences for each alternative identified?		X		Rehabilitation and patient costs were not adequately represented
4.1 Was the range wide enough for the research question at hand?	X			That of rehabilitation program and patients not considered
4.2 Did it cover all relevant viewpoints?	X			See above
4.3 Were capital costs, as well as operating costs, included?	X			Considered in hospital direct costs estimates
5. Were costs and consequences measured accurately in appropriate physical units?	X			Length of stay in hospital was not reported
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		See above
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?		X		None reported
6. Were costs and consequences valued credibly?			X	None reported
6.1 Were the sources of all values clearly identified?			X	
6.2 Were market values employed for changes involving resources gained or depleted?			X	
6.3 Where market values were absent were adjustments made to approximate market values?			X	
6.4 Was the valuation of consequences appropriate for the question posed?			X	
7. Were the costs and consequences adjusted for differential timing?		X		No discounting reported
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		See above
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			Incremental costs presented
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		Not consequences, this was cost analysis
9. Was a sensitivity analysis performed?		X		No sensitivity analysis reported
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		Discussion limited and inadequate for Drummond criteria
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio provided
10.2 Were the results compared with those of others who have investigated the same question?	X			Adequate comparisons
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		Limited discussion regarding generalizability
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Current smokers display increased costs, hospitalizations were higher amongst drop-outs
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?		X		None provided

Drummond Review - Levin *(1991)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**No perspective identified**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Only Costs considered
1.2 Did the study involve a comparison of alternatives?	X			Standard care compared to intervention
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No perspective identified
2. Was a comprehensive description of competing alternatives given?	X			Well described alternatives
2.1 Were any important alternatives omitted?		X		None
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care group utilized
3. Was there evidence that the programmes' effectiveness had been established?		X		Non randomized design reduces the value of evidence of effectiveness
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		Non-randomized design
4. Were all the important and relevant costs and consequences for each alternative identified?			X	Out-patient visits to other hospitals not included – difficult to assess impact
4.1 Was the range wide enough for the research question at hand?			X	See above
4.2 Did it cover all relevant viewpoints?	X			Limited viewpoint – should have considered broader societal perspective
4.3 Were capital costs, as well as operating costs, included?	X			Incorporated into hospital charges
5. Were costs and consequences measured accurately in appropriate physical units?	X			Costs appear to be measured accurately
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		None appear omitted
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?		X		No such issues
6. Were costs and consequences valued credibly?			X	No sources provided
6.1 Were the sources of all values clearly identified?		X		No sources were provided making it difficult to assess credibility of methods utilized
6.2 Were market values employed for changes involving resources gained or depleted?			X	
6.3 Where market values were absent were adjustments made to approximate market values?			X	
6.4 Was the valuation of consequences appropriate for the question posed?			X	
7. Were the costs and consequences adjusted for differential timing?	X			Discount rate of 5% utilized
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?	X			Costs only
7.2 Was any justification given for the discount rate used?		X		None provided
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			Costs only
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		Incremental cost reported
9. Was a sensitivity analysis performed?	X			Sensitivity analysis conducted around the discount arte 0-10%
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?		X		None provided
9.2 Were study results sensitive to changes in the values?		X		No changes to findings
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			Good discussion provided
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio provided
10.2 Were the results compared with those of others who have investigated the same question?	X			Good discussion of previous literature
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			Various patterns of return to work reported from country to country limiting the potential generalizability of these findings
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Effects of anxiety and depression significant to return to work
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	X			Authors suggest a C/E or C/U analysis is required to establish conclusive findings regarding economic value

Drummond Review - *Pilote (1992)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**No mention of costs but rather effectiveness**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Only hospitalizations and income considered
1.2 Did the study involve a comparison of alternatives?	X			Intervention compared to usual care
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		Not stated but appears to be a limited societal viewpoint
2. Was a comprehensive description of competing alternatives given?	X			Adequate description
2.1 Were any important alternatives omitted?		X		No
2.2 Was (should) a do nothing alternative (be) considered?	X			UC was a comparator
3. Was there evidence that the programmes' effectiveness had been established?		X		No evidence of programs effectiveness was provided
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?		X		RCT design but no results to support effectiveness
4. Were all the important and relevant costs and consequences for each alternative identified?	X			Limited range and perspective
4.1 Was the range wide enough for the research question at hand?		X		The range was limited to hospitalizations and income
4.2 Did it cover all relevant viewpoints?		X		Rehabilitation costs not adequately accounted for. Only income was utilized to reflect patient perspective – there are other associated costs.
4.3 Were capital costs, as well as operating costs, included?			X	We are unable to assess if overhead was included
5. Were costs and consequences measured accurately in appropriate physical units?	X			Units were accurate and appropriate for question
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		None omitted
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?		X		None reported
6. Were costs and consequences valued credibly?		X		No monetary assignment of cost applied
6.1 Were the sources of all values clearly identified?				N/A
6.2 Were market values employed for changes involving resources gained or depleted?				N/A
6.3 Where market values were absent were adjustments made to approximate market values?				N/A
6.4 Was the valuation of consequences appropriate for the question posed?				N/A
7. Were the costs and consequences adjusted for differential timing?		X		No discounting
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		See above
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?	X			Only hospital costs
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		See above
9. Was a sensitivity analysis performed?		X		None performed
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?		X		See above
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		Adequate discussion of findings and implications
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No ratio provided
10.2 Were the results compared with those of others who have investigated the same question?	X			Adequate comparisons made
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		Emphasis place do CABG via study population
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Emphasize importance of physician buy-in
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?		X		Changes to guidelines causes difficulties, wide latitude in interpretation of guidelines

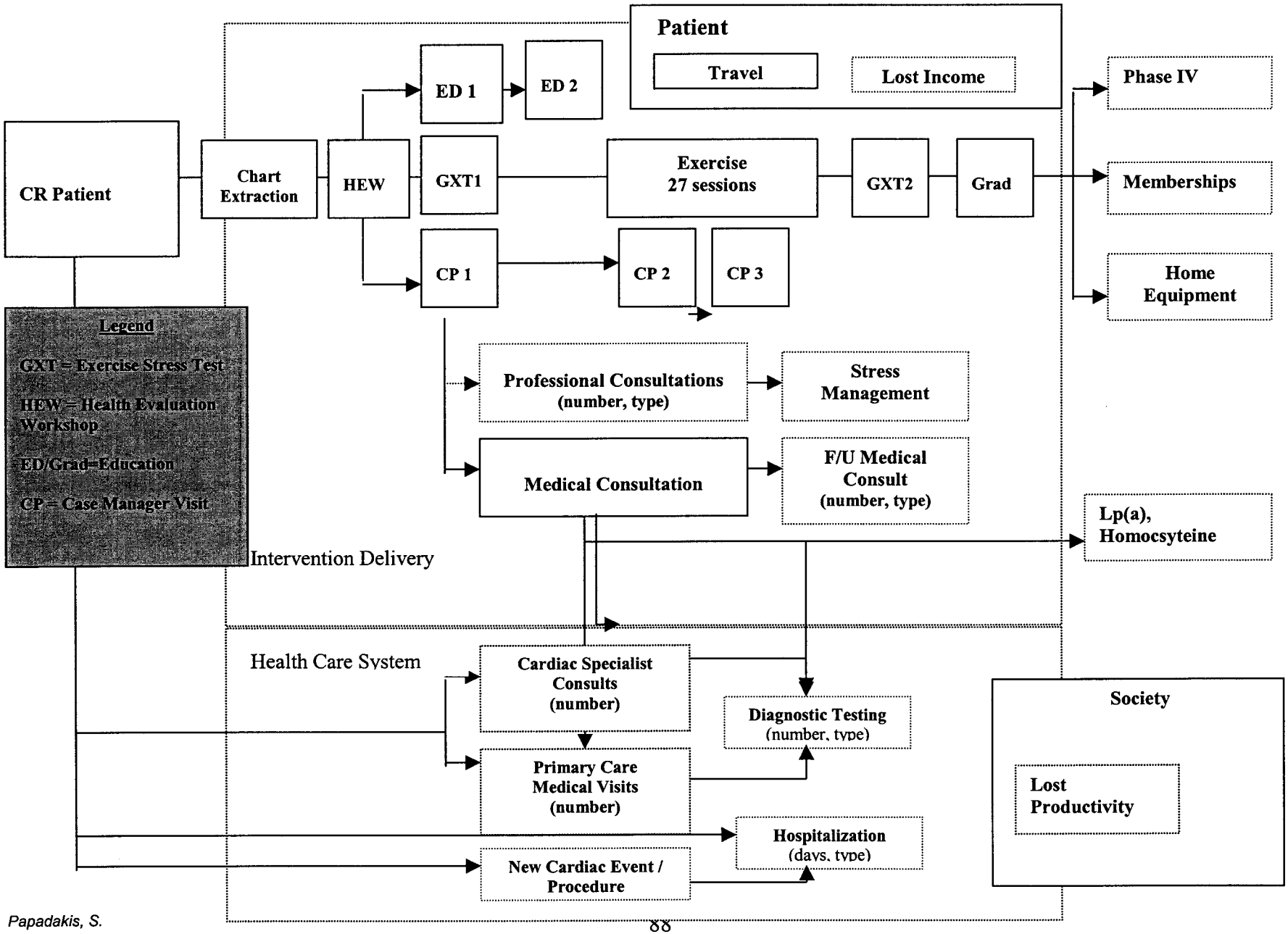
Drummond Review - *Picard (1989)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**Question posed lacks sufficient clarity**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Only costs were evaluated
1.2 Did the study involve a comparison of alternatives?	X			Intervention vs. control
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		No viewpoint has been explicitly stated
2. Was a comprehensive description of competing alternatives given?	X			An adequate description of this simple intervention provided
2.1 Were any important alternatives omitted?		X		
2.2 Was (should) a do nothing alternative (be) considered?	X			Control group design was used
3. Was there evidence that the programmes' effectiveness had been established?	X			
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			
4. Were all the important and relevant costs and consequences for each alternative identified?	X			
4.1 Was the range wide enough for the research question at hand?	X			
4.2 Did it cover all relevant viewpoints?		x		
4.3 Were capital costs, as well as operating costs, included?	X			Provided within estimated of direct hospital costs
5. Were costs and consequences measured accurately in appropriate physical units?	X			
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		Patient perspective considered only in part
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	X			Multiple hospitals utilized
6. Were costs and consequences valued credibly?	X			Valued credibly
6.1 Were the sources of all values clearly identified?	X			
6.2 Were market values employed for changes involving resources gained or depleted?	X			
6.3 Where market values were absent were adjustments made to approximate market values?	X			
6.4 Was the valuation of consequences appropriate for the question posed?				N/A
7. Were the costs and consequences adjusted for differential timing?		X		No discounting
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		
9. Was a sensitivity analysis performed?	X			Sensitivity analysis conducted around one variable charges for hospitalization
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?	X			Charges between there hospitals involved in the study
9.2 Were study results sensitive to changes in the values?		X		Robustness remained
10. Did the presentation and discussion of study results includes all issues of concern to users?	X			
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		None provided
10.2 Were the results compared with those of others who have investigated the same question?	X			Minimal comparative research published
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?	X			Authors state generalizability is difficult to assess but may be applicable to other non cardiac settings as well
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Number of MI patients who could benefit form intervention would translate into large societal benefits
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?		X		

Drummond Review - *DeBusk (1985)*

Checklist Question	Yes	No	Can't Tell	Discussion
1. Was a well-defined question posed in an answerable form?		X		**Question does not explicitly state economic evaluation was conducted**
1.1 Did the study examine both costs and effects of the service(s) or programme(s)?		X		Program delivery costs and effectiveness are evaluated as separate analyses
1.2 Did the study involve a comparison of alternatives?	X			Home training compared to group training
1.3 Was a viewpoint for the analysis stated and was the study placed in any particular decision making context?		X		Not explicitly stated within the publication but is that of the rehabilitation program
2. Was a comprehensive description of competing alternatives given?	X			A very detailed overview of the intervention is presented
2.1 Were any important alternatives omitted?		X		
2.2 Was (should) a do nothing alternative (be) considered?	X			Standard care comparison for effectiveness
3. Was there evidence that the programmes' effectiveness had been established?	X			RCT established program effectiveness
3.1 Has this been done through a randomized, controlled clinical trial? If not, how strong was the evidence of effectiveness?	X			Strong evidence of equivalent effects between group on cardiovascular outcomes
4. Were all the important and relevant costs and consequences for each alternative identified?		X		The perspective selected and range of costs is severely limited and doe not reflect the additional societal costs of the interventions under evaluation
4.1 Was the range wide enough for the research question at hand?		X		The evaluation of costs was limited to direct rehabilitation expenses and did not report patient or health care costs which would be influenced
4.2 Did it cover all relevant viewpoints?		X		Only that of the rehabilitation program is evaluated
4.3 Were capital costs, as well as operating costs, included?		X		Equipment was included but not overhead and rent.
5. Were costs and consequences measured accurately in appropriate physical units?		X		The lack of inclusion of rent an overhead for the home and exercise group is limiting and would underestimate the cost of delivering such a program in other settings
5.1 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?		X		None
5.2 Were there any special circumstances (e.g. joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?	X			The costing data assumes that the home program uses office facilities already dedicated to a similar purpose such as supervised training in YMCA programs
6. Were costs and consequences valued credibly?			X	Despite the clear description of logic to support unit measures for costs no description of values for identified costs was provided
6.1 Were the sources of all values clearly identified?			X	No sources were identified for costs
6.2 Were market values employed for changes involving resources gained or depleted?		X		Unable to assess
6.3 Where market values were absent were adjustments made to approximate market values?			X	Unable to assess
6.4 Was the valuation of consequences appropriate for the question posed?		X		Consequences were not assessed
7. Were the costs and consequences adjusted for differential timing?		X		No discounting reported
7.1 Were the costs and consequences which occur in the future 'discounted to their present values?		X		See above
7.2 Was any justification given for the discount rate used?				N/A
8. Was an incremental analysis of costs and consequences of alternatives performed?		X		No incremental comparison conducted
8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits or utilities generated?		X		Reported for groups – no incremental value reported
9. Was a sensitivity analysis performed?		X		None performed
9.1 Was justification provided for the ranges of values employed in the sensitivity analysis?				N/A
9.2 Were study results sensitive to changes in the values?				N/A
10. Did the presentation and discussion of study results includes all issues of concern to users?		X		The discussion around economic evaluation was minimal. The emphasis was placed on the efficacy of the interventions under comparison,
10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g. cost effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?		X		No index reported
10.2 Were the results compared with those of others who have investigated the same question?		X		No economic studies would be available for comparison
10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?		X		The study references only the interventions applicability to MI patients
10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration?	X			Adherence rates between groups discussed. Home program identified as potentially more convenient for participants.
10.5 Did the study discuss issues of implementation, such as the feasibility of adopting the 'preferred' programme given existing financial other constraints, and whether any freed resources could be redeployed to other worthwhile programmes?	X			The authors note that further research is required to evaluate which form of cardiac rehabilitation program is most cist-effective.

Appendix 5: Treatment Path Schemata



Appendix 6: OVERVIEW OF KEY STUDY VARIABLES

Resource Identification	**Unit of Measurement**	**Method of Measurement**	**Cost Valuation**
Operating Costs			
Exercise Equipment	Number and type	Inventory	Financial Records
Medical Equipment	Number and type	Inventory	Financial Records
Overhead / Accommodation	Percentage of total costs	Compliance	14% & 30%
Program Delivery Costs			
Professional staff time	Hours by vocation	CRF record	Annual Wages
Fixed CR Test	Number and type of test	Compliance	Cost per test
Materials and Supplies	Number of workshops	Compliance	Financial Records
Health Care Utilization			
Cardiac Tests	Number and Type	Study questionnaire	OHIP
Cardiac Procedures	Number and type	Study questionnaire	JPPC
Hospitalizations	Number of Hospitalizations / days	Study questionnaire	JPPC
Cardiac Specialist Visits	Number	Study questionnaire	OHIP
General Practitioner Visits	Number	Study questionnaire	OHIP
Medical Specialist Visits	Number	Study questionnaire	OHIP

Analysis Variables

Variable	**Details**	**Quantification**
Cardiac Risk Strata	Low / Moderate / High	CACR and AACVPR risk strata tools
Cardiac Diagnosis	CABG / PTCA / MI / Angina	Study database
Age	Categorical	Date of Birth
Gender	Male / Female	Reported
Program Completion	>80% attendance	Exercise Logs
Possible QoL Benefits to Derive	QALY<1.0	TTO

HIPRC, Heart Institute Prevention and Rehabilitation Financial Records
JPPC, Joint Policy and Planning Committee, Reports
OHIP, Ontario Health Insurance Program Schedule of Benefits

Appendix 7: DATA COLLECTION QUESTIONS

Data Collection Questions
QALYs
TTO (10 / 20 / 30)
Visual Analog scale (0-100)
Health Care System (CAD related costs)
Additional Hospital Resources (specialist consultations) Ottawa Civic Hospital Cost Model
Primary Care services (estimated using OHIP schedule of benefits)
Medical Test / Procedures (1-month period prior to study follow-up)
Morbidity / Mortality
Study Questionnaire
Health Care Perspective
Have you had an appointment with you family physician in the last month? (Y/N) IF yes how many times in the last month have you met with your family physician?
Have you had an appointment with your cardiac specialist in the last month? (Y/N) IF yes how many times in the last month have you met with your cardiac specialist?
Have you been in contact with any other doctors in the last month If yes specify physicians name and how many times.
Have you been hospitalized since your last study follow-up? (Y/N) If yes, please indicate the number of days in total you were in hospital.
Have you undergone any medical procedures or surgeries since your last study follow-up? (Y/N). Please specify.
Societal Perspective / Patient Perspective
Are you currently employed? (Y/N)
If you have returned to work since your last study follow-up please indicate the approximate date you returned to work. (mm/dd/yyyy)
Approximately how many days have you been absent from work in the past month?
If you have stopped working since your last study follow-up please indicate the approximate date you stopped working. (mm/dd/yyyy)
Patient Perspective
Are you currently participating in a community based cardiac rehabilitation program or other exercise program? (Y/N)
Are you currently a member of a gym or fitness club? (Y/N) If yes, do you (pay per visit, have a 1, 3, 6, 12 month membership)? If yes, please indicate the approximate cost of your membership. Less than $100 $100-$250 $251-$500 More than $500
Have you purchased any exercise equipment since your last study follow-up? (Y/N)
If Yes, please indicate the approximate value of the equipment purchased. Less than $99 $100 to $499 $500 to $999 $1000 or more

Appendix 8: Cost and Sources Utilized in the Valuation of Health Services

Program Delivery Costs

Professional Salaries

Vocation	Hourly	Minute	Source
Mean	$ 39.03	$ 0.651	HIPRC
Physio	$ 37.12	$ 0.619	HIPRC
Dietician	$ 37.12	$ 0.619	HIPRC
Social Work	$ 40.40	$ 0.673	HIPRC
Vocational	$ 35.99	$ 0.600	HIPRC
Psychology	$ 43.66	$ 0.728	HIPRC
Nursing	$ 39.90	$ 0.665	HIPRC

Exercise Sessions	Mean	Per Contact	Source
Exercise Class	$115.53/1.5hour	$ 5.78	Salaries
Equipment		$ 2.13	HIPRC Purchase Records
Overhead	14% / 30%		UOHI Finance Dept.

Medical Visits	Mean	Min	Source
Assessment	$ 112.35		HIPRC / OMA
Follow-up	$ 57.1	$ 25.15	HIPRC / OMA

Health Services

Hospitalization

DRG	Mean	Min	Source
Angina	$ 1,008.71	$ 145.00	JPPC
Heart Failure	$ 2,724.99	$ 113.00	JPPC
Emergency	$ 164.45	$ 73.85	OMA
MI	$ 3,642.00	$ 271.00	JPPC
CABG	$ 12,600.00		OMA
PTCA	$ 2,034.00		JPPC
PTCA with STENT	$ 4,784.00		JPPC
Cost/STENT	$ 1,500.00		JPPC
STENT Mean	$ 2,750.00		JPPC
Cardioversion	$ 64.70		OMA
Endartorectomy	$ 3,019.00		JPPC
Valve Surgery	$ 3,691.00		OMA
AAA	$ 10,443.00		OMA
Pacemaker	$ 3,136.00	$ 1,945.00	JPPC

Diagnostic Tests

Category	Mean	Min	Source
Blood Test	$ 14.49		Dept of Path & Lab Med
Urine Test	$ 4.20		OMA
X-ray	$ 150.00		OMA
Echo / Ultrasound	$ 95.90		OMA
ECG	$ 150.00		OMA
Ex.Myoview	$ 270.00		OMA
Pers. Myoview	$ 580.00		OMA
GXT	$ 163.00	$ 231.00	OMA
Angiogram	Left or right $ 725.00	Left & right $ 847.00	JPPC
MRI	$ 102.65		OMA
CT Scan	$ 102.00		OMA
Holter	$ 123.90		OMA
Perfusion	$ 21.95		OMA
Diffusion	$ 102.00		OMA

Physician Visits

Profession	Mean	Min	Source
Cardiology	$ 112.02		OMA
General Practitioner	$ 54.75	$ 29.95	OMA
Specialist	$ 112.02		OMA

HIPRC, Heart Institute Prevention and Rehabilitation Financial Records
JPPC, Joint Policy and Planning Committee, Reports
OHIP, Ontario Health Insurance Program Schedule of Benefits
OMA, Ontario Medical Association

Appendix 9: Time-Trade-off (TTO) Script

Visual Analog Question:
Where would you rank your current health on this scale, if 0 represents death and 100 represents perfect health?

Perfect Health
100
90
80
70
60
50
40
30
20
10
0
Death

Time Trade-off Question:
Let's assume your life expectancy is 20 years. I am going to give you some choices and ask which you prefer.

Choice 1 is to live your remaining 20 years in your current health state

Choice 2 is to live a shorter time but in perfect health. Let's say in Choice 2 you get to live 10 years in perfect health.

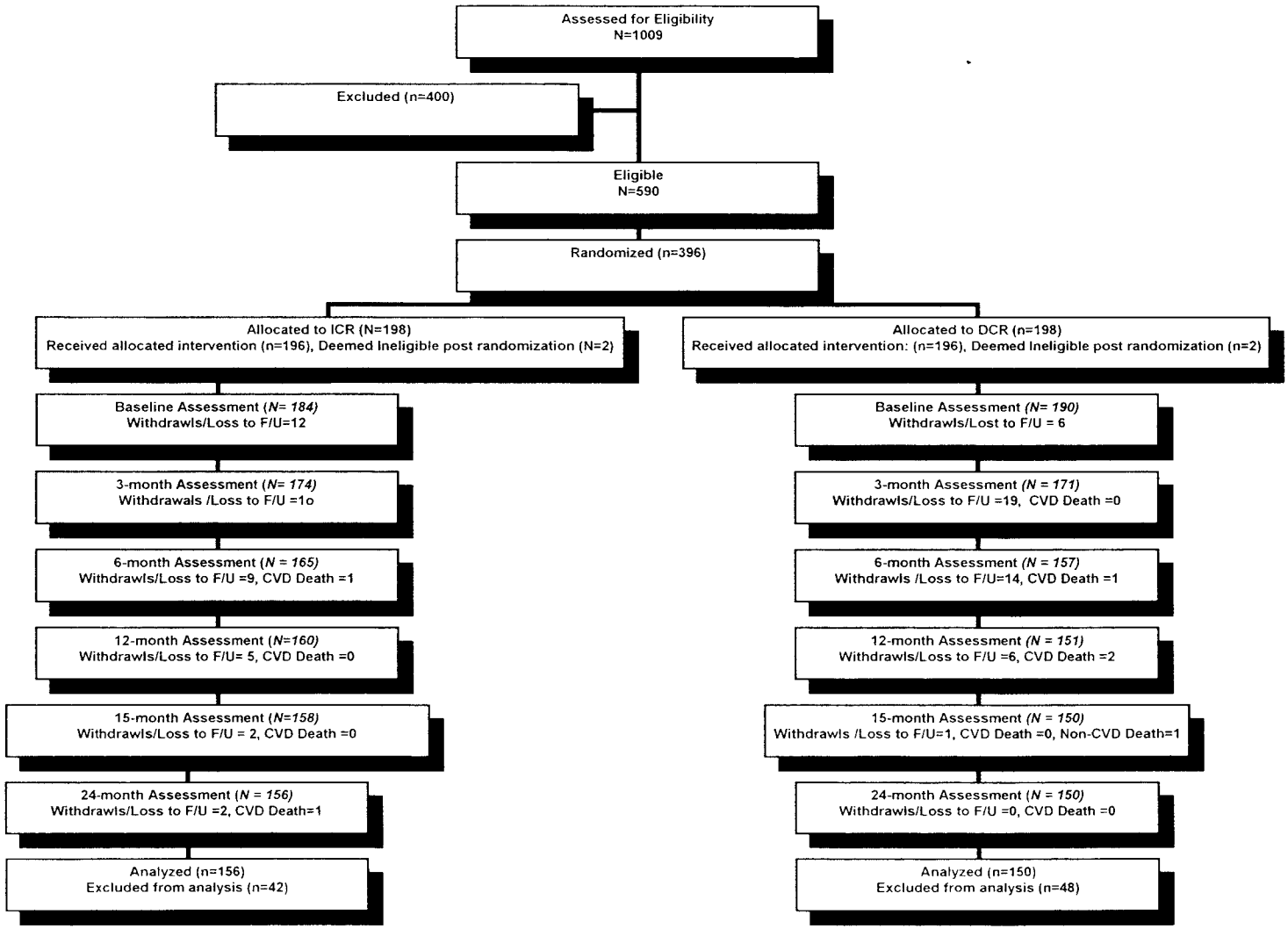
Choice 1
20 years in your
Current Health

Choice 2
10 years in Perfect
Health

Which would you take? Choice 1, or Choice 2?

Depending on choice, the participant then repeats the process with higher (choice 2) or lower (choice 1) years of perfect health.

Appendix 10: Overview of Study Recruitment and Follow-up



Appendix 11: Characteristics of Active and Inactive Study Participants

Patient Characteristic	Active N=306	In-Active N=90	P Value
Mean Age (SD)	58.3 (9.71)	56.3 (11.7)	ns
Gender % Male % Female	 89.3 10.7	 76.7 23.3	 .003
Cardiac Diagnosis* % CABG % PTCA % MI % Angina	 11.9 45.4 6.5 36.2	 19.8 37.2 10.5 32.6	 ns
Mean Years Education (SD)	15.0 (4.1)	13.7 (4.1)	.014
Cardiac Acute Risk Strata ** % High % Moderate % Low	 20.5 50.5 29.0	 16.9 37.3 45.8	 .015

* Admitting primary cardiac diagnosis ** AACVPR risk stratification for acute risk of exercise complications

Appendix 12: Bootstrap Probability Table

Proportion of replications producing a positive net benefit for the 3-month intervention arm at each of the threshold values

Threshold Value for a QALY	Proportion of replications with positive net benefit
$ 0	0.630
$ 5,000	0.646
$ 10,000	0.657
$ 15,000	0.660
$ 20,000	0.666
$ 25,000	0.665
$ 30,000	0.666
$ 35,000	0.667
$ 40,000	0.664
$ 45,000	0.663
$ 50,000	0.661
$ 55,000	0.660
$ 60,000	0.658
$ 65,000	0.654
$ 70,000	0.652
$ 75,000	0.65
$ 80,000	0.648
$ 85,000	0.646
$ 90,000	0.645
$ 95,000	0.643
$ 100,000	0.642

Appendix 13: Monte Carlo Simulation

Recalculated mean costs following sensitivity analysis using Monte Carlo simulation

Variable	3-month	12-month	b-a
Professional Staff Time			
Exercise sessions	$144.21	$144.41	$0.20
Contact Person Visits	$98.61	$97.47	($1.14)
Counseling Sessions	$99.75	$137.69	$37.94
Stress Management	$22.80	$37.67	$14.87
Medical Consults	$220.07	$237.40	$17.33
Equipment	$49.30	$49.37	$0.07
Operating costs	$73.83	$81.94	$8.11
Total Program Delivery	**$708.57**	**$785.95**	$77.38
CABG	$565.38	$420.00	($145.38)
PTCA	$433.92	$496.73	$62.81
MI	$70.05	$72.85	$2.80
Other Cardiac*	$133.03	$198.23	$65.20
Unspecified**	$525.41	$739.56	$214.15
Emergency Visits	$21.99	$21.76	($0.23)
Cardiac Diagnostic	$1,037.28	$321.78	($715.50)
Physician Services			$0.00
General Practitioner	$482.14	$436.77	($45.37)
Cardiac Specialist	$493.96	$437.32	($56.64)
Other Specialists	$548.49	$527.99	($20.50)
Total Health Care	**$4,311.65**	**$3,672.98**	($638.66)
Total Costs	**$5,020.22**	**$4,458.93**	($561.29)
QALY Gain	0.06	0.05	($0.01)
Cost/QALY	$82,958.66	$9,657.02	($73,301.64)

Note: Highlighted variables have been adjusted to reflect uncertainty

References

1. *The Changing Face of Heart Disease in Canada 2000.* 1999, Heart and Stroke Foundation of Canada.

2. Agency for Health Care Policy and Research, *Clinical Practice Guideline: Cardiac Rehabilitation.* 1995, Rockville, MD: US Department of Health and Human Services.

3. Jolliffe, J., et al., *Exercise-based rehabilitation for coronary heart disease (Cochrane Review).* In: The Cochrane Library, 2003(1).

4. O'Connor, G., et al., *An overview of randomized trials of rehabilitation with exercise after myocardial infarction.* Circulation, 1989. **80**(2): p. 234-244.

5. Oldridge, N., et al., *Cardiac rehabilitation after myocardial infarction: combined experience of randomized clinical trials.* JAMA, 1988. **260**(7): p. 945-950.

6. Oldridge, N., et al., *Effects on quality of life with comprehensive rehabilitation after acute myocardial infarction.* Am J Cardiol, 1991. **67**(13): p. 1084-9.

7. Oldridge, N., *Predictors of health related quality of life with cardiac rehabilitation after acute myocardial infarction.* Journal of Cardiopulmonary Rehabilitation, 1998. **18**: p. 95-103.

8. Goldman, L., et al., *Task Force 6. Cost Effectiveness of Assessment and Management of Risk Factors.* J Am Coll Cardiol, 1996. **27**(5): p. 964-1047.

9. Garard, K., I. Smoker, and J. Seymour, *Raising the quality of cost-utility analyses: lessons learnt and still to learn.* Health Policy, 1999. **46**: p. 217-238.

10. Goldman, L., et al., *Cost-effectiveness of assessment and management of risk factors.* Journal of the American College of Cardiology, 1996. **27**: p. 1020-1030.

11. Drummond, M., et al., *Methods for the Economic Evaluation of Health Care Programs, 2nd Edition.* 1997, Oxford: Oxford University Press.

12. Kupersmith, J., et al., *Cost-effectiveness analysis in heart disease, Part I: General principles.* Prog Cardiovasc Dis, 1994. **37**(3): p. 161-84.

13. Oldridge, N.B., *Comprehensive cardiac rehabilitation: is it cost-effective?* Eur Heart J, 1998. **19 Suppl O**: p. O42-50.

14. Klassen, T.P., A.R. Jadad, and D. Moher, *Guides for reading and interpreting systematic reviews: I. Getting started.* Arch Pediatr Adolesc Med, 1998. **152**(7): p. 700-4.

15. Jadad, A.R., D. Cook, and G. Browman, *A guide to interpreting discordant systematic reviews.* Can Med Assoc J, 1997. **156**: p. 1411-1416.

16. Mulrow, C., D. Cook, and F. Davidoff, *Systematic reviews: Critical links in the great chain of evidence.* Annals of Internal Medicine, 1997. **126**(5): p. 389-391.

17. Moher, D. and I. Olkin, *Meta-analysis of randomized controlled trials: a concern for standards.* JAMA, 1995. **274**: p. 1962-4.

18. Chalmers, I. and B. Haynes, *Reporting, updating, and correcting systematic reviews of the effects of health care*, in *Systematic Reviews*, I. Chalmers and D. Altman, Editors. 1995, BMJ: London. p. 86-95.

19. Chalmers, T.C. and I. Lau, *Meta-analytic stimulus for changes in clinical trials.* Stat Methods Med Res, 1993. **2**: p. 161-72.

20. Oxman, A., *Undertaking systematic reviews of research effectiveness: CRD guidelines for those carrying out or commissioning reviews*. 1996, The Cochrane Collaboration: Oxford.

21. Sutton, A., et al., *Systematic reviews and meta-analysis: a structured review of the methodological literature.* J Health Serv Res Policy, 1999. **4**(1): p. 49-55.

22. Verhagen, A., et al., *The art of quality assessment of RCTs included in systematic reviews.* Journal of Clinical Epidemiology, 2001. **54**: p. 651-654.

23. Stone, J.A., et al., *Canadian guidelines for cardiac rehabilitation and cardiovascular and atherosclerotic heart disease prevention: a summary.* Can J Cardiol, 2001. **17 Suppl B**: p. 3B-30B.

24. Brown, A., et al., *Exercise-based cardiac rehabilitation programs for coronary artery disease: a systematic clinical and economic review.* 2003, Canadian Coordinating Office for Health Technology Assessment: Ottawa.

25. DeBusk, R.F., et al., *Medically directed at-home rehabilitation soon after clinically uncomplicated acute myocardial infarction: a new model for patient care.* Am J Cardiol, 1985. **55**(4): p. 251-7.

26. Levin, L.A., J. Perk, and B. Hedback, *Cardiac rehabilitation--a cost analysis.* J Intern Med, 1991. **230**(5): p. 427-34.

27. Ades, P.A., D. Huang, and S.O. Weaver, *Cardiac rehabilitation participation predicts lower rehospitalization costs.* Am Heart J, 1992. **123**(4 Pt 1): p. 916-21.

28. Edwards, W., et al., *Percutaneous transluminal coronary angioplasty rehabilitation: A cost-effective analysis.* J Cardiopulm Rehabil, 1993. **13**: p. 172-181.

29. Oldridge, N., et al., *Economic evaluation of cardiac rehabilitation soon after acute myocardial infarction.* Am J Cardiol, 1993. **72**(2): p. 154-61.

30. Bondestam, E., A. Breikss, and M. Hartford, *Effects of early rehabilitation on consumption of medical care during the first year after acute myocardial infarction in patients > or = 65 years of age.* Am J Cardiol, 1995. **75**(12): p. 767-71.

31. Allison, T.G., et al., *Medical and economic costs of psychologic distress in patients with coronary artery disease.* Mayo Clin Proc, 1995. **70**(8): p. 734-42.

32. Ades, P.A., F.J. Pashkow, and J.R. Nestor, *Cost-effectiveness of cardiac rehabilitation after myocardial infarction.* J Cardiopulm Rehabil, 1997. **17**(4): p. 222-31.

33. Garattini, L., et al., *A proposal for Italian guidelines in pharmacoeconomics.* Pharmacoeconomics, 1995. **7**(1): p. 1-7.

34. Russell, L.B., et al., *The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine.* JAMA, 1996. **276**(14): p. 1172-7.

35. Torrance, G., et al., *Canadian Guidelines for Economic Evaluation of Pharmaceuticals.* Pharmacoeconomics, 1996. **9**(6): p. 535-559.

36. Glennie, J., et al., *The revised Canadian guidelines for the economic evaluation of pharmaceuticals.* Pharmacoeconomics, 1999. **15**(5): p. 459-468.

37. Grobler, M., et al., *Industry comment on the 1995 revised Australian pharmacroeconomic guidelines.* Pharmacoeconomics, 1996. **9**: p. 353-356.

38. Rovira, J. and F. Antonanazas, *Economic analysis of health technologies and programmes. A spanish proposal for methodological standardization.* Pharmacoeconomics, 1995. **8**(3): p. 245-252.

39. Baladi, J., *A guidance document for the costing process.* 1996, Canadian Coordinating Office for Health Technology Assessment (CCOHTA): Ottawa.

40. CCOHTA, *Guidelines for economic evaluation of pharmaceuticals: Canada - 2nd Edition.* 1997, Canadian Coordinating Office for Health Technology Assessment: Ottawa.

41. Shephard, R.J., *Economic benefits of secondary and tertiary cardiac rehabilitation: a critical study.* Ann Acad Med Singapore, 1992. **21**(1): p. 57-62.

42. Honey, E., et al., *Cost effectiveness of screening for Chlamydia trachomatis: a review of published studies.* Sex Transm Infect, 2002. **78**(6): p. 406-12.

43. Drummond, M., et al., *Use of pharmacoeconomics information--report of the ISPOR Task Force on use of pharmacoeconomic/health economic information in health-care decision making.* Value Health, 2003. **6**(4): p. 407-16.

44. Georgiou, D., et al., *Cost-effectiveness analysis of long-term moderate exercise training in chronic heart failure.* Am J Cardiol, 2001. **87**(8): p. 984-8; A4.

45. Lowensteyn, I., et al., *The cost-effectiveness of exercise training for the primary and secondary prevention of cardiovascular disease.* J Cardiopulm Rehabil, 2000. **20**(3): p. 147-55.

46. Robertson, M.C., et al., *Economic evaluation of a community based exercise programme to prevent falls.* J Epidemiol Community Health, 2001. **55**(8): p. 600-6.

47. Collins, L., P. Scuffham, and S. Gargett, *Cost-analysis of gym-based versus home-based cardiac rehabilitation programs.* Aust Health Rev, 2001. **24**(1): p. 51-61.

48. Carlson, J.J., et al., *Program participation, exercise adherence, cardiovascular outcomes, and program cost of traditional versus modified cardiac rehabilitation.* Am J Cardiol, 2000. **86**(1): p. 17-23.

49. Nieuwland, W., et al., *Differential effects of high-frequency versus low-frequency exercise training in rehabilitation of patients with coronary artery disease.* J Am Coll Cardiol, 2000. **36**(1): p. 202-7.

50. van Dixhoorn, J.J. and H.J. Duivenvoorden, *Effect of relaxation therapy on cardiac events after myocardial infarction: a 5-year follow-up study.* J Cardiopulm Rehabil, 1999. **19**(3): p. 178-85.

51. Thomas, R., N. Miller, and C. Lamendola, *National survey on gender differences in cardiac rehabilitation in cardiac rehabilitation programs: patient characteristics and enrollment patterns.* Journal of Cardiopulmonary Rehabilitation, 1996. **16**(6): p. 402-412.

52. Lavie, C. and R. Milani, *Effects of cardiac rehabilitation and exercise training on exercise capacity, coronary risk factors, behavioural characteristics, and quality of life in women.* American Journal of Cardiology, 1995. **75**(5): p. 340-343.

53. Scott, L., K. Ben-Or, and J. Allen, *Why are women missing from outpatient cardiac rehabilitation programs? A review of multi-level factors affecting referral, enrollment, and completion.* J Womens (Larchmt), 2002. **11**(9): p. 773-91.

54. Halm, M., *Women and cardiac rehabilitation: referral and compliance patterns.* J Cardiovasc Nurs, 1999. **13**(3): p. 83-92.

55. Brezinka, V. and F. Kittel, *Psychological factors of coronary heart disease in women: a review.* Soc. Sci. Med., 1996. **42**(10): p. 1351-65.

56. Pilote, L., et al., *Return to work after uncomplicated myocardial infarction: a trial of practice guidelines in the community.* Ann Intern Med, 1992. **117**(5): p. 383-9.

57. Picard, M.H., et al., *Cost-benefit analysis of early return to work after uncomplicated acute myocardial infarction.* Am J Cardiol, 1989. **63**(18): p. 1308-14.

58. Brubaker, P.H., et al., *Comparison of standard- and extended- length participation in cardiac rehabilitation on body composition, functional capacity, and blood lipids.* American Journal of Cardiology, 1996. **78**: p. 769-773.

59. Morrin, L., S. Black, and R. Reid, *Impact of duration of a cardiac rehabilitation program on coronary risk profile and health related quality of life.* Journal of Cardiopulmonary Rehabilitation, 2000. **20**: p. 115-121.

60. Jadad, A.R., D. Moher, and T.P. Klassen, *Guides for reading and interpreting systematic reviews: II. How did the authors find the studies and assess their quality?* Arch Pediatr Adolesc Med, 1998. **152**(8): p. 812-7.

61. Moher, D., A.R. Jadad, and T.P. Klassen, *Guides for reading and interpreting systematic reviews: III. How did the authors synthesize the data and make their conclusions?* Arch Pediatr Adolesc Med, 1998. **152**(9): p. 915-20.

62. Robertson, K.A. and K. Kayhko, *Cost analysis of an intensive home follow-up program for first-time post-myocardial infarction patients and their families.* Dynamics, 2001. **12**(4): p. 25-31.

63. Belardinelli, R., et al., *Randomized, controlled trial of long-term moderate exercise in chronic heart failure.* Circulation, 1999. **99**: p. 1173-1182.

64. O'Brien, B.J. and M.F. Drummond, *Statistical versus quantitative significance in the socioeconomic evaluation of medicines.* Pharmacoeconomics, 1994. **5**(5): p. 389-98.

65. Briggs, A.H., *Handling uncertainty in cost-effectiveness models.* Pharmacoeconomics, 2000. **17**(5): p. 479-500.

66. Probstfield, J., *How cost-effective are new preventive strategies for cardiovascular disease?* Am J Cardiol, 2003. **91**(suppl): p. 22G-27G.

67. Oldridge, N., *Cardiac rehabilitation exercise programme compliance and compliance enhancing strategies.* Sports Medicine, 1988. **6**: p. 42-55.

68. Prosser, G., P. Carson, and R. Philips, *Exercise after myocardial infarction: long-term rehabilitation effects.* Journal of Psychosomatic Research, 1985. **29**(5): p. 535-540.

69. Daltroy, L., *Improving cardiac patient adherence to exercise regimes: a clinical trial of health education.* Journal of Cardiopulmonary Rehabilitation, 1985. **5**: p. 40-49.

70. Prochaska, J., C. DiClemente, and J. Norcross, *In search of how people change; applications too addictive behaviours.* American Psychologist, 1992. **9**: p. 1104-1114.

71. Houston-Miller, N. and C.B. Taylor, *Lifestyle management in patients with coronary heart disease.* 1995, Champlain, IL: Human Kinetics.

72. *A methodology for costing and an approach to funding pacemakers and implantable cardioverter defibrilators: Final report.* 1999, Joint Policy and Planning Committee (JPPC).

73. *Cardiac funding working group final report: A programmatic appraoch to funding cardiac & cardiology procedures.* 1997, Joint Policy and Planning Committee (JPPC).

74. Ontario Ministry of Health, *OHIP Billing Schedule.* 2002.

75. Raisch, D.W., *Understanding quality-adjusted life years and their application to pharmacoeconomic research.* Ann Pharmacother, 2000. **34**(7-8): p. 906-14.

76. Brown, G.C., et al., *Quality of life associated with diabetes mellitus in an adult population.* J Diabetes Complications, 2000. **14**(1): p. 18-24.

77. Cheng, A.K., et al., *Cost-utility analysis of the cochlear implant in children.* JAMA, 2000. **284**(7): p. 850-6.

78. Efron, B. and G. Gong, *A leisurely look at the bootstrap, the jacknife, and cross-validation.* The American Statitician, 1983. **37**(1): p. 36-48.

79. Briggs, A.H., *Handling Uncertainty in economic evaluation and presenting the results*, in *Economic evaluation in health care*, M. Drummond and A. McGuire, Editors. 2001, Oxford University Press: Oxford.

80. Laupacis, A., et al., *How attractive does a new technology have to be to warrant adoption and utilization? Tenative guidelines for using clinical and economic evaluations.* Can Med Assoc J, 1992. **146**(4): p. 473-481.

81. Laupacis, A., *Inclusion of drugs in provincial drug benefit programs: who is making these decisions, are they the right ones?* JAMA, 2002. **166**(1): p. 44-47.

82. Chapman, R., et al., *A comprehensive league table of cost-utility ratios and a sub-scale of "panel worthy" studies.* Med Decis Making, 2000. **20**(4): p. 451-67.

83. Goel, V., R. Deber, and A.S. Detsky, *Nonionic contrast media: economic analysis and health policy development.* Can Med Assoc J, 1989. **140**: p. 389-395.

84. Morocutti, G., D. Tuniz, and P.M. Fioretti, *Comprehensive cardiac rehabilitation: an issue to be readdressed.* Eur Heart J, 1999. **20**(20): p. 1448-1450.

85. Earle, C., et al., *Systematic overview of cost-utility assessments in oncology.* J Clin Oncology, 2000. **18**: p. 3302-3317.

86. Revicki, D. and R. Kaplan, *Relationship between psychometric and utility-based approaches to the measurement of health-related quality of life.* Qual Life Res, 1993. **2**: p. 477-87.

87. Revicki, D., N. Leidy, and F. Brennan-Diemer, *Integrating patient preferences into health outcome assessment: the multi-attribute Asthma symptom utility index.* Chest, 1998. **1998**(114): p. 998-1007.

88. Ware, J. and C. Sherbourne, *The Medical Outcomes Study, SF-36 item short form health survey (SF-36) conceptual framework and item selection.* Med Care, 1992. **30**: p. 473-482.

89. Oldridge, N.B., *Outcome assessment in cardiac rehabilitation. Health-related quality of life and economic evaluation.* J Cardiopulm Rehabil, 1997. **17**(3): p. 179-94.

90. Brazier, J., J. Roberts, and M. Deverill, *The estimation of a preference-based measure of health from the SF-36.* J Health Econ, 2002. **21**(2): p. 271-92.

91. Hawthorne, G., J. Richardson, and N. Day, *A comparison of the assessment of quality of life with four other generic utility instruments.* Ann Med, 2001. **33**: p. 358-70.

92. Longworth, L. and B. Stirling, *An empirical comparison of EQ-5D and SF-6D in liver transplant patients.* Health Econ, 2002.

93. Conner-Spady, B. and M. Suarez-Almazor, *Variation in the estimation of quality-adjusted life years by different preference-based instruments.* Med Care, 2003. **41**(7): p. 791-801.

94. O'Brien, B.J., et al., *A view from the bridge: agreement between the SF-6D utility algorithm and the Health Utilities Index.* Health Econ, 2002.

95. Brazier, J., et al., *Deriving a preference-based single index from the UK SF-36 Health Survey.* J Clin Epidemiol, 1998. **51**(11): p. 1115-28.

96. Torrance, G.W., W.H. Thomas, and D.L. Sackett, *A utility maximization model for evaluation of health care programs.* Health Serv Res, 1972. **7**(2): p. 118-33.