THE COST-EFFECTIVENESS OF AN ADAPTED COMMUNITY-BASED AEROBIC WALKING PROGRAM FOR INDIVIDUALS WITH MILD OR MODERATE OSTEOARTHRITIS OF THE KNEE

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ABSTRACT

This thesis investigated the cost-effectiveness of a 12-month supervised aerobic walking program with or without a behavioural intervention and an educational pamphlet, compared to an unsupervised/self-directed educational pamphlet intervention, among individuals with moderate osteoarthritis (OA) of the knee. Analyses included an economic evaluation to assess the cost effectiveness of the two walking interventions from both the societal and Canadian provincial/territorial health care payer perspectives. A value of information analysis exploring the potential value of future research was also performed. Results revealed that the unsupervised/self-directed intervention was the most cost-effective approach given that it cost the least to implement and participants had higher quality-adjusted life years (QALYs). Walking, either supervised in a community setting, or unsupervised in a setting such as the home, may be a favourable non-pharmacological option for the management of OA of the knee. The thesis concludes with a policy discussion relating to the funding of non-pharmacological therapies.

ACRONYMS AND ABBREVIATIONS

ACR	American College of Rheumatology
AIMS-2	Arthritis Impact Measurement Scales 2
ALF	Aggregate locomotor function score
BMI	Body mass index
C	Self-directed walking intervention
CCS	Comparative controlled study
CCT	Controlled clinical trial
CEAC	Cost-effectiveness acceptability curve
CSRI	Client Services Receipt Inventory
CPDD	Calcium pyrophosphate-deposition disease
CUA	Cost-utility analysis
EQ-5D	EuroQol-5 Dimension Questionnaire
ESCAPE	Enabling Self-management and Coping with Arthritic Knee Pain through Exercise
EVPI	Expected Value of Perfect Information
HAD	Hospital Anxiety and Depression score
HRU	Health resource utilization
HsW	Health-sector-Wide
ICER	Incremental cost-effectiveness ratio
INB	Incremental net benefit
IRGL	Impact of Rheumatic Diseases on General health and Lifestyle index
LHIN	Local health integration networks
MAR	Missing at random
MCAR	Missing completely at random
MET	Total metabolic equivalent
NHS	National Health Service
NMB	Net monetary benefit
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International

OKS	Oxford Knee Score
PA	Physical activity
PACEex	Program for Arthritis Control through Education and Exercise
PAR	Physical activity recall
PHAC	Public Health Agency of Canada
PICO	Population, Intervention, Comparison, and Outcome
PTA	Percutaneous transluminal angioplasty
QALY	Quality-adjusted life year
QOL	Quality of life
RCT	Randomized controlled trial
SD	Standard deviation
SE	Standard error
SF-36	Short Form (36) Health Survey
SF-6D	Short Form Six-Dimension utility index
SMART	Senior's Maintaining Actives Roles Together program
TAS	The Arthritis Society
VAS	Visual analogue scale
W	Supervised walking intervention
WB	Supervised walking and behavioural intervention
WTP	Willingness to pay
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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Chapter I

IINTRODUCTION AND BACKGROUND

The following chapter outlines the objective and structure of this thesis. The chronic condition of osteoarthritis (OA), its burden on the Canadian population, and risk factors that are associated with the joint disorder are introduced. The concept and importance of an economic evaluation is discussed to highlight the purpose of this thesis. Lastly, evidence suggesting how physical activity (PA), such as a walking program, may improve OA symptoms is presented to support of the interventions used in this study.

1.1 Introduction

1.1.1 Statement of the problem

As individuals age they start to develop more health complications. OA is a degenerative disease resulting from the biochemical breakdown of articular cartilage in the synovial joints. The word osteoarthritis is derived from the Greek word "*osteo*", meaning bone, "*arthro"*, meaning joint, and "*itis"* meaning inflammation (1). OA, the most common arthritic condition, affects approximately three million Canadians and one in 10 individuals in the general population (2).By the age of 70, it is estimated that 85% of Canadians will be affected by osteoarthritis (3). OA is one of the leading causes of functional limitations in the elderly and affects 10% of Canada's population (4). The most apparent complications that arise from this disease that worsens over time are chronic pain and physical disability. The quality of life (QOL) of these individuals can deteriorate because of their loss of motility. Individuals may experience joint stiffness and pain and may find it difficult to perform everyday tasks. In some cases individuals find it too strenuous to continue working (5). The major causes of knee OA are obesity, joint injury or

overuse, inactivity and lack of physical exercise, joint wear and tear and hereditary gene defect (5).

Aside from physical and psychological impairments that reduce QOL, the large socio-economic burden on health services is a significant negative consequence caused by OA (6). Individuals who suffer from OA are more likely to use health-care services more frequently when compared to a representative group of adults (7). It is estimated that by the year 2020, the prevalence of individuals who live with disabilities caused by OA will double, adding significantly to the economic burden on health care services (8) (9). Researchers believe that the costs of arthritic disorders may potentially exceed other popular medical illnesses and complications including cardiovascular disease (10).

1.1.2 Objectives

The overall aim of this project was to assess the cost-effectiveness of a community-based aerobic walking program for OA of the knee through a single-blind randomized controlled trial (RCT). The primary purpose of this project was to analyse the effects of training on QOL, resource utilization and the long-term effects on cost and quality adjusted life expectancy at 12, 15, and 18 months.

1.1.3 Relevance to research

In order for both health care providers and health policy makers to make evidence-based decisions regarding the most cost-effective interventions, further investigation is required to obtain a valid estimate of the cost-utility and cost-benefit of non-pharmacological interventions

for OA of the knee. In rheumatology, the science of economic evaluation is not adequately developed to compellingly reveal the cost effectiveness of treatments (11). Therapeutic exercise and PA are the most commonly prescribed non-pharmacological interventions by health professionals (12). The cost-analyses of these types of interventions have not been thoroughly examined and therefore an economic evaluation for an aerobic walking program was needed.

1.1.4. Outline

This chapter provides a thorough background, causes and risk factors, and the economic burden of OA. The second chapter provides a thorough systematic review of the literature pertinent to cost-effective exercise interventions for individuals with OA of the knee. The third chapter outlines the methods used to develop the community-based aerobic walking program study, how the participants were assessed, and how the cost-utility analysis (CUA) was performed. Chapter four will present the results of the CUA. The fifth chapter, divided into two parts, considers the significance of the findings while demonstrating the relationship of the previous results with the literature. The second part of the fifth chapter discusses policy implications relating to considerations of who should pay for non-pharmacological interventions and offers suggestions for future research.

1.2 Background

1.2.1 Osteoarthritis

There are over 100 different types of arthritis and joint diseases that have been classified into categories depending on the grade of swelling, infection and haemorrhage. Each type of arthritis is unique and has different signs, symptoms, diagnostic and prognostic criteria, and methods of

treatment (13). OA affects the weight-bearing components of the joint such as the menisci, bone and articular cartilage. At the chronic stage of this disease, the joint space of the knee becomes narrow, resulting in irritation and inflammation of the joint synovial membrane, causing an increase in synovial fluid, swelling, tenderness, and pain (13).

1.2.2. Causes and Risk Factors of Osteoarthritis

There are several other known risk factors of OA that can be characterized into three different categories: biological and genetic factors, environmental and occupational factors, and social and behavioural factors.

More than 80% of Canadians over the age of 70 develop OA (14). The elderly are at greater risk of developing OA as a result of joint wear and tear (15) and natural changes in growth factors functions within joints that may complicate cartilage healing and new bone formation (16). As individuals age, the water content in cartilage increases and the protein makeup begins to degenerate causing the cartilage to flake or form crevasses (17). OA, along with other age associated morbidities, will continue to contribute to the impact of disability and will worsen the QOL of the elderly population (18).OA occurs more frequently in men among individuals below the age of 45 (19) and more frequently in women after the age of 55 (20). Women experience greater muscle and joint pain given that females have a lower proportion of lean mass and a higher percentage of body fat content, increasing the rate of muscle fatigue (21). OA is more prevalent among Caucasians and African Americans when compared to other ethnic groups (22).

Several diseases and complications can contribute to and may increase the risk developing OA. Calcium pyrophosphate-deposition disease (CPDD), also called "chondrocalcinosis" or "pseudogout", is a common disorder among the elderly which creates deposits of calcium containing crystals in joint tissues. The monitoring of CPDD among several large families has shown that this disorder progresses into severe degenerative OA (23).

Several endocrine disorders such as diabetes, acromegaly, hypothyroidism and hyperparathyroidism affect the musculoskeletal system and may disrupt primary changes in bone and collagen resulting in secondary arthritis and bone changes (24). Several metabolic disorders that are known to cause biochemical or genetic abnormalities such as hemochromatosis, ochronosis, Wilson's disease, sickle cell anemia, and thalassemia have all shown to be causative factors that may produce OA (25). Some bone diseases such as Paget's disease and osteopetrosis can induce changes in bone elasticity, possibly forming osteoarthritis (25). Several dysplasias including familial polyepiphyseal dysplasia, congenital spondyloepiphyseal dysplasia, Stickler's syndrome, osteo-onychodysplasia, Kniest's dysplasia, trichorhinopharyngeal syndrome, and a group of diseases that affect the epiphyses all show to be causative factors of OA (25). In endemic areas of the world, disorders known as Mselini disease, Kashin-Beck disease, and Malnad disease, have been identified to be responsible for premature OA (25).

Hereditary joint defects have shown to increase the development of OA. Abnormality in a gene responsible for the production of collagen can lead to the breakdown of cartilage, leading to joint defects, such as bow legs (varus position) and knock knees (valgus position), as well as hip dislocation or laxity (also known as double-jointed) (1). A genetic abnormality known as Ehlers-

Danlos syndrome is a specific example of a genetic defect that may contribute to the development of OA. Ehlers-Danlos syndrome induces joint laxity in which patients display hypermobility of the joints which may complicate the articular cartilage and elastic tissue in the body, potentially developing into OA (26).

Obesity has a direct correlation to the development of knee OA as excess weight causes strain on the joints, increasing the probability of joint damage (27). With each additional 10 pounds of weight, the force on the knees of an overweight adult increases by 30 to 60 pounds with each step (28)

Race and ethnicity are other biological and genetic factors that may contribute to the prevalence of OA. OA of the knee has shown to be more prevalent among African American women than other groups (29). Separate studies have revealed that African-Americans are more likely to develop OA in both knees (30) and that Asian women are at increased risk of developing OA of the knee when compared to Caucasian Americans (31).

Occupational risk factors such as carrying and lifting heavy weights and working while in a posture that requires kneeling or squatting may contribute to the development and progression of OA (32). Male construction workers, specifically male masons and agriculture workers of both sexes are more likely to develop OA of the hip or knee (33). The overuse of joints, especially among athletes and labourers who subject their knees to ongoing stress and strain during their young adult and middle-aged years are at greater risk of developing OA (34). Athletes in sports

such as basketball, football, or soccer, who experience repeated knee injuries, harming the internal tissues of a joint, are more likely to develop osteoarthritis as they get older (34).

Physical inactivity can be just as harmful to the joints as it weakens and deteriorates the muscles which support the joints and decreases joint flexibility. In time, a sedentary lifestyle and underused joints from inactivity will cause stiffness, pain, dysfunction, and more susceptibility to injury and OA (34). Diet is another important risk factor for OA development as a low intake of vitamin D has shown to promote joint space narrowing and increase the risk of the progression of knee OA (35). Individuals who consume high doses of vitamin C in their diet developed severe OA of the knee and may aggravate cartilage damage (36). Level of education has been associated with OA prevalence as 41% of adults with less than a high school education reported having OA compared to 21% of college graduates (22).

1.2.3 The Economic Burden of Osteoarthritis

The costs of the management of OA are very high since it is a chronic condition that is very prevalent and incurable (12). The costs per individuals who suffer from OA are small. However, the costs at the population level are large because of the joint disease's high prevalence (37).The cost of arthritis in 1998 was estimated at 4.4 billion Canadian dollars which accounted for over one-quarter of the total costs of musculoskeletal dieases, and 10.3% of the total economic vurden of all illnesess in Canada (38). More recently, in 2004, it was estimated that the total societal costs associated with OA specifically were approximately 3.26 billion Canadian dollars (39). A study which measured the economic burden of OA among individuals in Ontario revealed that the average total annual costs, both health care and non-health care costs, incurred by these

individuals were $12 200 (40). The sources of health care costs which are more substantial include hospital care and surgery facilities (41).

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Evidence shows that non-health care costs such as time lost from employment, time unable to perform household chores and unpaid caregiver time spent on household chores also plays a major role in the economic burden of individuals with OA (40). It appears as though health care costs exceed non-health care costs as the majority of individuals who suffer from OA are retired or no longer participate in labour market activities which results in fewer non-health care costs related to employment (7). Contrary to this, Gupta et al. (40) found that non-health care costs are the main cause of the economic burden of OA after considering that non-health care costs are not only incurred by individuals with OA, but are split between those attributable to their caregivers as well. It is evident that as health status declines and OA severity increases, individuals are more inclined to incur higher costs (40). A study conducted by Gabriel et al. (11) concluded that individuals with OA spent more on medical costs (US $2044) than the controls who did not have OA (US $1592). Maetzel et al. (39) revealed that 7.9% of individuals with OA purchased adaptive aids and 82.9% had at least one investigative test during the 6 month study period.

1.2.4 Economic Evaluation

The purpose of an economic evaluation is to assist decision makers compare the costs and benefits of health care interventions when making decisions regarding the allocation of scarce resources (42). The costs recorded in an economic evaluation are the value of changes in resource use as a result of the intervention (43). Whilst ideally studies should adopt a societal perspective, economic evaluations are usually from the perspective of the health care system.

The most common form of analysis is a CUA, an analysis which measures the additional cost per quality-adjusted life year (QALY) gained (43). QALY is a measure of disease burden which includes both the quantity and the quality of life lived (44). It provides a value to treatments which allows for comparisons to be made between new and existing interventions (44). The QALY score is a representation of the amount of time spent in a particular health state which is weighted by the utility score given to that health state (44).The utility score of a specific health state is given a numeric value between 0 and 1 to represent the QOL in which 0 represents death and 1 represents "perfect health" (44). For example, an individual who requires a wheel chair, a QALY score of 0.37 (45), for 3 years would result in QALY score of 1.11.

1.2.5 Physical Activity Interventions and Osteoarthritis

The Ottawa Panel recently developed clinical practice guidelines for therapeutic exercises and manual therapy in the management of OA (46), for weight management among obese and overweight individuals with OA (47), and for aerobic walking programs in the management of OA (48). Common therapeutic exercise interventions include both muscle strengthening and aerobic PA. Results from this meta-analysis illustrated that included RCTs (49) (50) (51) (52) (53) (54) (55) (56) (57) (58) and a controlled clinical trial (CCT) (59) ,which examined a walking program versus a non-walking control, confirmed both clinically important and statistically significant improvements in QOL, functional status, energy level and aerobic capacity among the intervention groups.

PA such as functional or aerobic exercise, at either a high or low intensity can improve functional status, pain, gait, and aerobic capacity (60) (46) among OA patients. Bicycling and

strengthening exercises enhances health and may prevent disability and functional loss. PA can increase muscle strength (61) and improve mobility, specifically stair climbing (58) (62) (63) (64) (65). Therapeutic exercise consisting of range of motion exercises, are believed to be beneficial for joints because they increase synovial fluid circulation providing nutrients for articular cartilage. In addition, PA has shown to reduce pain by increasing endogenous opioid content in brainstem regions which are important for pain modulation (66).

PA can potentially reduce disability and improve QOL by minimizing the severity and functional impact of OA (52), improving pain relief (67) and facilitating weight management by improving cardio-respiratory fitness (68). PA has shown to be an effective intervention for preventing injuries, specifically in reducing falls among seniors by improving training in balance, strength, co-ordination and reactions (69). Exercise can improve flexibility and endurance which are essential for preventing injuries (70).

Chapter II

SYSTEMATIC REVIEW OF ECONOMIC EVALUATION STUDIES USING AEROBIC EXERCISE INTERVENTIONS FOR KNEE OA

The following chapter presents a systematic review of RCTs which conducted an economic evaluation alongside studies which included an aerobic exercise intervention for individuals with OA of the knee.

2.1 Objective

The aim of this systematic review was to examine studies which reported cost-effectiveness of aerobic exercise in treatment of osteoarthritis of the knee. In addition, the purpose of the review was to reveal the strengths and limitations of similar studies, drawing on lessons in order to facilitate the research of this thesis.

2.2 Methods

The systematic review was conducted using the PICO (Population, Intervention, Comparison, and Outcome) framework (71) (72) in order to facilitate the literature search and improve precision (73). The PICO framework is a useful tool for performing an effective search strategy as it helps identify key concepts of the research question (74).

The patient population that was included in the systematic search were individuals suffering from any form of OA, which broadened the search. The interventions that were selected included aerobic walking and aerobic exercise therapy, interventions similar to the aerobic walking program used in the study that will be analyzed in the following chapters. In regards to comparisons, no specific intervention was chosen as a comparator, again allowing for a broadened search. The outcome measures that were included in the search were: QOL, health

care resource utilization or any studies which have performed a cost-effectiveness or cost- utility analysis. The detailed search strategy is presented in Appendix 2.1.

Five databases: Medline, Embase, The Cochrane Library, the National Institute for Health Research Economic Evalaution Database, and the Center for Evaluation of Value and Risk in Health Cost-Effectiveness Analysis Registry were used in the systematic literature search. In addition, recent conference proceedings from 2004- June 2011were also searched using the Web of Science web site index (http://thomsonreuters.com/products_services/science/science_products/a-z/conf_proceedings_citation_index). Search results were then transferred to an online reference management program RefWorks (www.refworks.com), where duplicate results were organized and removed. The identified articles were screened based on their abstracts and full texts were obtained for closer inspection. Articles were included if they reported on a comparative controlled study (CCS) using an aerobic exercise intervention for the treatment of knee OA. Included articles must have been presented in a scientifically valid manner and must have reported results of an economic evaluation including costs and health care utilization.

The methodological quality of the included CCSs was assessed using the elements of a sound economic evaluation. (75). The criteria were used to identify and compare the strengths and weaknesses of each study. The criteria are illustrated as a suggested checklist containing 10 questions (Table 2.1).Quality was assessed by two reviewers (GD and DC). Differences were solved through consensus. Results of the quality assessment are described in the following section and summarized in Table 2.1.

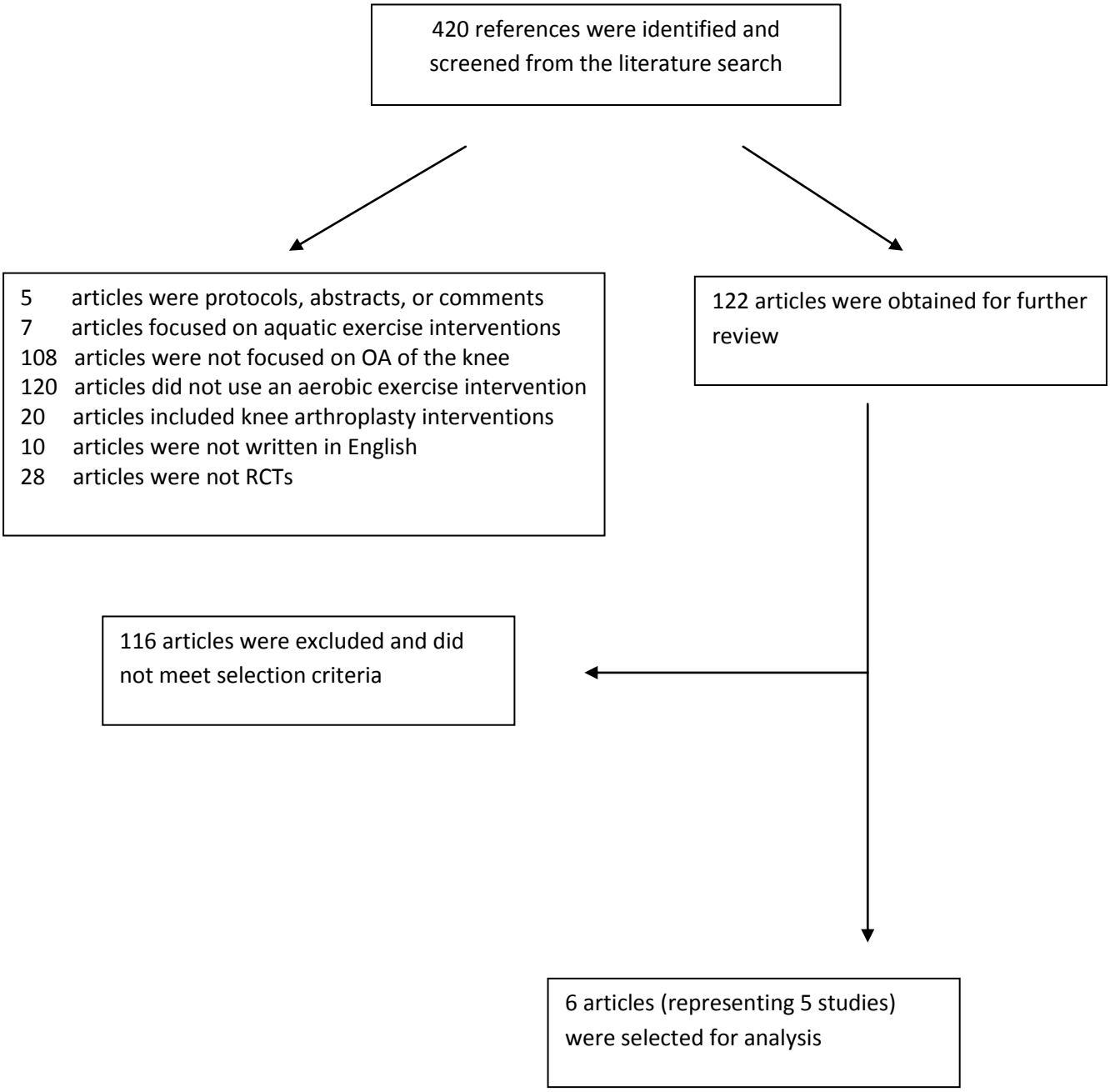
Table 2.1 Drummond et al. Suggested Checklist for Assessing Economic Evaluations for the Included Studies

	Hurley et al., 2007			Jessep et al., 2009			Sevick et al., 2000			Richardson et al.,2006 / McCarthy et al. 2004			Thomas et al., 2005		
Criteria	**GD**	**DC**	**Consensus**	**GD**	**DC**	**Consensus**	**GD**	**DC**	**Consensus**	**GD**	**DC**	**Consensus**	**GD**	**DC**	**Consensus**
Was a well-defined question posed in answerable form?	X	X	X	X	X	X	X	X	X	X	X	X		X	X
Was a comprehensive description of the competing alternatives given?	X	X	X	X	X	X	X	X	X	X	X	X		X	X
Was there evidence that the programme's effectiveness had been established?	X	X	X		X	X	X	X	X	X	X	X	X	X	X
Were all the important and relevant costs and consequences for each alterative identified?	X	X	X		X	X	X	X	X	X	X	X			
Were costs and consequences measured accurately in appropriate physical units?	X	X	X				X	X	X	X	X	X	X		
Were costs and consequences valued credibly?	X	X	X	X	X	X	X	X	X	X	X	X	X		
Were costs and consequences adjusted for differential timing?	X	X	X	NA	NA	NA	X	X	X	X	X	X			
Was an incremental analysis of costs and consequences of alternatives performed?	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Was a sensitivity analysis performed?	X	X	X				X	X	X	X	X	X	X	X	X
Did the presentation and discussion of study results include all issues of concern to users?	X	X	X	X			X	X	X	X	X	X			

2.3 Results

The systematic literature searched identified 420 publications in which 6 articles (2 represented the same study) were deemed to fulfill the inclusion criteria (See table 2.2). Publications were excluded if they were 1) uncontrolled studies; 2) studies using non-aerobic exercise interventions; 3) consisted of a specific population not representative of the general public (e.g. obese); 4) did not provide any economic information. Moreover, publications were excluded if they were letters, editorials, reviews or primary prevention studies. Studies using a surgical intervention (arthroplasty) or aquatic aerobic exercise interventions were excluded. Due to the limitations of time and translation costs, publications not written in English were also excluded. A narrative review of the included studies is provided in the following section with abstracts provided in the same format as the Centre for Reviews and Dissemination provided in Appendix 2.2. In addition, excluded studies which may provide additional information and lessons are described briefly in Section 2.6.

Figure 2.1 Flow chart showing the various steps of study selection



2.4 Included Studies

2.41. Exercise vs. Usual primary care: Hurley et al., 2007

An economic evaluation was conducted on an exercise program from arthritic knee pain called "Enabling Self-management and Coping with Arthritic Knee Pain through Exercise (ESCAPE)" (76). The study took place in South East London, United Kingdom, and included 418 participants, aged 50 years or older, who reported mild, moderate or severe knee pain for greater than 6 months. The interventions included usual primary care, usual primary care plus a rehabilitation program (ESCAPE) delivered individually and usual primary care plus the ESCAPE program delivered in a group. The rehabilitation programs consisted of 12 sessions, twice weekly for 6 weeks. Each session included 10 to 15 minutes of advice and coping strategies followed by 30 to 40 minutes of aerobic and functional exercises. The costs of both rehabilitation groups were compared to usual primary care and the costs of the individual rehabilitation intervention were compared to group rehabilitation intervention. The outcomes, measured at 6 months post-intervention, were self-reported functioning using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and QOL using the EuroQol (EQ-5D) instrument. The WOMAC function scores improved in both individual rehabilitation and group rehabilitation, and demonstrated a clinically meaningful improvement compared to usual care (121 of 226 compared to 47 of 113; χ^2 =4.301, p=0.038). There was no significant difference in utility value means [standard deviation (SD)] between individual rehabilitation 0.60 (0.29), group rehabilitation 0.60 (0.28) and usual care 0.60 (0.30). Results demonstrated no significant differences in mean health and social care costs 11£ (-23, 52) (95% confidence interval) between individual rehabilitation and group rehabilitation, and that both interventions were more costly than no rehabilitation. The ESCAPE program was argued to be cost effective

compared to usual care when measured by clinical outcomes of self-reported functional status and QOL. Missing data were minimized as the economic evaluation was conducted alongside the clinical trial. An important lesson learned from this study is to use valid measurement tools that will provide the most accurate results. The authors mentioned that the utility questionnaire that was used (EQ-5D) may be insensitive to measure QOL change and the trial was not powered to detect a significant change in this outcome.

Using the suggested checklist for assessing the methodological quality of economic evaluations (75)(Table 2.1), the study examined both costs and effects of the ESCAPE program. The study included a comparison (usual primary care) and stated the viewpoint of the analysis (health care, social care and societal perspective). The "usual primary care" control intervention was properly described, no alternatives were omitted, and a "do nothing" alternative was not necessary. The effectiveness of the ESCAPE program was previously established in previous publications (77) (78). In regards to important and relevant costs and consequences, the range was wide enough for the research question and covered all relevant viewpoints. Both capital costs and operating costs were included. No identified items were omitted from measurements. The sources of values were clearly identified (UK National health Service Executive hospital and community health services or personal social services national statistics) and the valuation of consequences showed to be appropriate in regards to the research question. The authors took discounting into consideration and noted that it was unnecessary due to the short assessment period. An incremental analysis of costs was performed comparing the intervention with the alternatives using cost-effectiveness acceptability curves (CEACs) based on QALYs. Two sets of sensitivity analyses were performed and the results showed to be sensitive to these changes. The first set

used alternative assumptions regarding the calculation of unit costs of rehabilitation (supervision by a junior therapist, reducing groups to 6 participants, increasing groups to 10 participants, both widening and narrowing cost difference by 50%). The second set tested the impact of alternative assumptions for the calculation of total health care and societal costs, which included travel time and costs. The authors' conclusions were interpreted intelligently, but were not compared to similar studies as they stated that it was the first study to evaluate the cost-effectiveness of an integrated exercise and self-management rehabilitation program to improve function among individuals with chronic knee pain. The study discussed the study results being generalizabile to an elderly, inner-city population and took into account the sensitivity issues of the EQ-5D questionnaire. It concluded that the program is a brief, affordable and cost-effective intervention.

2.4.2 Exercise vs. Outpatient physiotherapy: Jessep et al., 2009

A separate study (6) compared the clinical effectiveness and costs of the ESCAPE program to outpatient physiotherapy. The study was conducted in Sevenoaks, United Kingdom, and included 64 participants, who were 50 years of age or older, who had a diagnosis of OA of the knee, and who reported mild, moderate or severe knee pain for greater than 6 months. The ESCAPE program, previously described (Section 2.4.1), was delivered in a community centre, consisted of 10 sessions, twice weekly, and offered a review session four months after the completion of the program. Participants in the outpatient physiotherapy group underwent a maximum of 10 sessions where they were assessed for 30 to 45 minutes followed by treatment the physiotherapist felt necessary. The primary outcome, physical function, was assessed at baseline and 12 months using the WOMAC index. Health related QOL was assessed with the EQ-5D and health care utilization was assessed using the Client Services Receipt Inventory (CSRI). Results

of the ESCAPE program demonstrated physical improvements while being less costly. At the 12-month follow up, the individuals in the ESCAPE group had mean scores (SD) of 11.5 (12.1) for WOMAC function, 3.2 (3.3) for WOMAC pain, and 0.78 9(0.174) for EQ-5D while those in the outpatient physiotherapy group had mean scores of 12.2 (13.7) for WOMAC function, 4.2 (4.0) for WOMAC pain, and 0.73(0.23) for EQ-5D (p=0.035). The total mean (SD) cost of the ESCAPE program, assuming that six participants attend the complete program, was £319.71 (469) while the mean cost for the outpatient physiotherapy was £582.57 (1157). A major limitation of this study was its small sample size of only 64 individuals which the authors points out may have produced larger standard deviations and may have skewed the results. One must therefore be cautious when making inferences from the results of this study.

The study examined costs (Client Services Receipt Inventory) and effects (WOMAC & EQ-5D). It involved a comparison of an alternative (outpatient physiotherapy), but did not state the viewpoint of the analysis. No alternatives were omitted and a "do nothing" alternative was not necessary. The two interventions were well described. In this publication (6), the authors stated that the details of the ESCAPE program are published elsewhere, yet they did not mention any evidence of the program's effectiveness. Although the costs for each session of each intervention were given, the author's failed to explain what these cost consisted of (capital costs, professional fees, or equipment). It is also unclear from which viewpoint these costs are considered from. A lesson learned from this study is to not only use complete data for an analysis as valuable information could be lost. The cost source for the outpatient physiotherapy intervention was clearly identified as the authors stated that they were taken from the UK Department of Health database and were standardised to 2005 prices. The valuation of consequences, cost

effectiveness, was appropriate for the question posed. The use of discounting was not mentioned. An incremental cost effectiveness analysis was performed using the difference of intervention costs and the difference of EQ-5D data. A sensitivity analysis was not performed. The conclusion of the analysis is based on the results of the cost effectiveness ratio and seems to be interpreted properly. The results of the pain and function outcomes were compared with similar studies, but the costs results were not. The authors mentioned that the ESCAPE program demonstrates high adaptability and discussed the program's generalizability, stating that the program could produce considerable health care savings if it was extrapolated to a large population with chronic knee pain. Limitations including the small sample size and recall bias was taken into consideration in the discussion.

2.4.3 Individual Home-based exercise vs. Individual Home-based exercise supplemented with a Group exercise programme: Richardson et al., 2006 & McCarthy et al., 2004

An economic evaluation was performed alongside a pragmatic, single blind randomised clinical trial to determine cost-effectiveness of an individual home-based exercise programme versus a home-based exercise programme supplemented with an eight week class-based group exercise programme (79) (80). The study took place in Manchester, United Kingdom. A total of 214 participants were included in the study who were diagnosed with OA of the knee according to the American College of Rheumatology's (ACR) classification [reported knee pain, provided radiological evidence of OA, and experienced at least three of the following: 1) age greater than 50 years, stiffness for more than 30 minutes upon walking, 3) crepitus, 4) bony tenderness, 5) bony enlargement, 6) no palpable warmth] (81). Both groups were given an eight-week home exercise program which consisted of advice, an education session, and exercises aimed to reduce

muscle weakness and fatigue, and improve range of movement and standing balance. The treatment group participated in additional class-based exercises twice weekly for approximately 45 minutes. The home-based exercise program included sitting to standing exercises using a chair, quadriceps isometric contractions, knee extension and flexion exercises, and thigh, hip and calf stretches. The additional class-based exercise group participated in a circuit of exercises including a five-minute aerobic "shuttle walking test" warm-up, five minutes of stretching, five minutes of balance training using balance boards, 10 minutes of isotonic, functional, and weight bearing exercises, five minutes of isometric quadriceps exercises, and five minutes of a light aerobic walking to cool down. Outcome measures were recorded at baseline, and at 1, 6 and 12-month follow-ups. Outcome measures included physical dysfunction using the aggregate locomotor function score (ALF), pain using the visual analogue scale (VAS) and functional capacity using WOMAC, Short Form 36 Health Survey (SF-36), and EuroQol (EQ-5D). The home-based group demonstrated to be superior as there was an interaction pooled mean difference of -2.89 ($p<0.001$) in ALF scores, -14.9 ($p<0.001$) in VAS pain scores, and -3.39 ($p=0.03$) in the "physical function" domain of the WOMAC index. The class-based group had a superior mean SF-36 score for the "physical function" domain with a pooled mean difference of 5.61 ($p=0.005$). The class-based group had higher EuroQol health VAS thermometer scores with a mean difference of 0.4, but did not show statistical significance ($p=0.86$). The total costs per patient over the 12 month period for the class-based program was £440.04 and £445.52 for the home-based programme. The difference in utility values at 12 months was 0.05: 0.53 for the home-based programme and 0.58 for the class based programme. However, after adjusting for baseline utility, ALF, body mass index (BMI), age, gender and source of referral, the mean change in QALYs per patient over the 12-month period was 0.022 for the home-based

programme and 0.045 for the class-based programme, giving a mean difference of only 0.023. A lesson from this study is the importance of baseline adjustment for utility estimates. The analysis demonstrated that the class-based programme is likely to be more cost-effective as it was dominant, less costly and more effective in terms of QALYs.

The study examined both costs and effects of both the home-based and class-based exercise programmes. The analysis was taken from the perspective of the health provider [UK's National Health Service (NHS)]. The competing alternatives were properly described and no alternatives were omitted. A "do nothing" alternative was not considered and could have provided a valuable comparison. The evidence of the effectiveness of the program was shown and appeared to be strong. All relevant costs and consequences for each of the interventions were clearly identified and provided a wide enough range for the research question. The costs covered the NHS viewpoint and included capital and operating costs. Another lesson learned from this study is the need to perform probabilistic analysis in order to obtain true measures of uncertainty. The investigators used the missing at random (MAR) assumption and performed the multiple imputation technique to replace the missing values. There were no special circumstances that made measurements difficult. The cost sources of all values were clearly identified from cited national estimates which were inflated to 1999/2000 prices using the Health Service Cost index (82) (83). The authors (80) mentioned that discounting was unnecessary due to the short length of the intervention period. An incremental analysis was performed using incremental cost-effectiveness ratios (ICERs). Sensitivity analyses were performed which included travel costs and a complete case analysis where multiple imputation was used to replace each missing value. The results of the sensitivity analysis with the inclusion of travel costs demonstrated a marginal

impact at a willingness to pay (WTP) of £20, 000- £30,000 per QALY. The results of the complete case analysis did not alter any decision and demonstrated a marginal reduction in cost and a favourable QALY change of 0.12 for the class-based group. The conclusion of the analysis was based on ICERs and net monetary benefits (NMBs). The authors stated that there was a lack of literature regarding the cost-effectiveness of patient exercise programmes for OA and decided to compare their results to an economic evaluation of a primary care-based education programme for patients with OA (84) . Results of the Lord et al. (1999) study demonstrated no significant differences in outcomes and a significant increase in costs for the education programme. McCarthy et al. (2004) believed that this supported one of their hypotheses of general practioner-based patient education programmes not being cost-effective. The study mentioned that the effect of the treatments could be generalised to individuals with OA of the knee. The author's stated that the individual nature of the exercise programmes could potentially reduce generalizability and that a class effect may have occurred since the intervention was delivered to groups of patients as oppose to individually.

2.4.4 Resistance Exercise vs. Aerobic Exercise vs. Patient education: Sevick et al., 2000

Another cost-effectiveness study (85) for seniors with knee OA measured the differences between resistance exercise, aerobic exercise and an education control intervention. The study took place at two separate centres in Tennessee and North Carolina, U.S.A. It included 439 participants who were over the age of 60, provided radiographic evidence of knee OA, reported pain on most days of the month in at least one knee, and had difficulty performing everyday activities due to knee pain. The aerobic exercise training included a three-month facility-based program and a 15-month home-based program. The participants were encouraged to participate

in three one hour sessions per week. Each session consisted of a warm up involving stretching and a slow walk, followed by a walking stimulus phase where participants were asked to walk at an intensity using 50% to 70% of their maximum heart rate, and a cool down which included a slow walk and flexibility exercises. The home-based program took place immediately after the three-month facility program and consisted of home visits and telephone follow-up calls to participants by the program leader. Similar to the aerobic exercise program, the resistance exercise program also consisted of a three-month facility-based program and a 15- month home based program which were performed during three one-hour sessions per week. The resistance exercise program included nine exercises (leg extension, leg curl, step up, heel raise, chest fly, upright row, military press, biceps curl, and pelvic tilt) using dumbbells and cuff weights. Resistance weights were increased in a step-wise fashion. Home visits and telephone follow-ups were performed in the same fashion as the aerobic exercise intervention. A health education intervention was used as a control and consisted of a monthly 90 minute video presentation of OA topics during the first three months, contact by a nurse bi-weekly to discuss any OA issues during months 4 to 6, and monthly during months 7 to 18. Costs and outcome measures were then compared among the three different intervention groups. Outcome measures were performed at baseline, 6, 12 and 18 months and included self-reported disability using an investigator-developed questionnaire and physical performance using the 6-min walking distance, a timed stair climb/descent, a lift and carry task, and time required to get in and out of a car. Results demonstrated that the aerobic exercise had better mean scores adjusted for baseline values when compared with the health education group with incremental improvements of 0.18 points ($p<0.0001$) for self-reported physical disability, 158 feet ($p<0.0001$) for 6-min walking distance, 1.2 seconds ($p=0.05$) for stair climb/descent, 0.9 seconds ($p<0.0001$) for lifting and

carrying tasks and 1.9 seconds ($p<0.0001$) for car tasks. The resistance group also demonstrated better mean scores when compared to the health education group with incremental improvements of 0.16 points ($p<0.003$) for self-reported physical disability, 57 feet ($p=0.02$) for the 6-min walking distance, 0.7 seconds ($p=0.02$) for the stair climb/descent, 0.7 seconds ($p=0.001$) for lifting and carrying tasks and 1.6 seconds ($p=0.003$) for car tasks. The first lesson learnt from this study is that investigators need to incorporate multidimensional outcome measures in their studies. The cost of the aerobic intervention ($323.55) and the resistance exercise intervention ($325.20) did not cost as much as the educational intervention ($343.98). Compared to the aerobic exercise group, the resistance exercise group demonstrated greater incremental savings per incremental effect over the education group on the majority of the variables: $117 per point for the self-reported disability score ($p<0.003$), $33 per foot for the 6 minute walk test ($p=0.02$), $27 per second for stair climbing ($p=0.02$), $27 per second for the lifting and carrying task ($p=0.001$), and $12 per second for the car task ($p=0.003$). Another lesson learnt from this study is the need to compare all alternatives by a proper incremental analysis. Although resistance training was superior to control, the magnitude of the differences in efficiency between the two interventions was small leading to uncertainty if the results were clinically significant.

The study examined both costs and effects of aerobic exercise, resistance exercise, and health education groups. The viewpoint of the analysis was from a health care payer's perspective. The three interventions were well described and no important alternatives were omitted. Since a health education control was selected, a "do nothing" alternative was not necessary. Evidence of the programme's effectiveness was demonstrated through the RCT and demonstrated statistically significant results ($p< 0.05$). The range of costs and consequences were wide enough for the

research question and the costs covered the specified viewpoint (health care payer). Both capital and operating costs were considered as the cost model included physician fees, in-center activities, fitness club memberships, home visit fees by an exercise instructor, travel costs, telephone service fees, and costs associated with adverse events. All costs and consequences were measured accurately and none of the identified items were omitted from measurement. A special circumstance took place which involved the death of one participant while travelling from her vehicle to the intervention. Since the death was unlikely related to the intervention, the costs associated with this event were excluded from the analysis. The cost source for physician services was clearly identified from a credible source, the 1994 Medicare physician fee schedule, but other costs such as health clubs membership fees, telephone service fees, and counselling sessions with a nurse were estimated using community surveys. The authors stated that since the purpose of the trial was to compare the effects of the two exercise interventions, they chose to estimate the participant's expected expenses rather than actual expenses from the program. Although these calculations seem to be appropriate, the accuracy of these estimations is unknown. It was stated that discounting was unnecessary due to the short duration of the intervention period. Two incremental cost-effective analyses were performed comparing the aerobic exercise program with the health education program. The second analysis compared the resistance exercise program to the health education program. A sensitivity analysis was conducted which assumed no adverse event occurred during both exercise intervention, resulting in a minimal influence on the incremental cost and did not change any conclusions. The conclusions of the analysis were based on total and incremental costs which were interpreted intelligently. The author's stated that although they did not use the most precise approach to estimate the total costs, it may be generalizable to pragmatic settings. The results were not

compared to other studies. The authors took into consideration that the economic analysis was performed *post hoc* and that a traditional accounting approach for calculating the cost of care in conjunction with the trial may have provided more accurate results.

2.4.5 Home-based exercise vs. Monthly telephone support: Thomas et al., 2005

The cost-effectiveness of a two-year individual home exercise program for pain treatment for knee OA was assessed (86). The study was conducted in Nottingham, United Kingdom and included 786 participants, men and women, aged 45 years and over with self-reported knee pain. The study compared 4 different treatment groups: exercise therapy, monthly telephone support, exercise combined with telephone support, and no intervention. The exercise programme intervention was delivered by a research nurse in participants' homes which was designed to improve muscle strength, range of motion and locomotor function and consisted of quadriceps strengthening using graded resistance elastic bands and aerobic exercises. Within the first two months, individuals participated in four 30 minute training sessions and were then encouraged to perform the exercises for 20 to 30 minutes daily by recording their performances in a diary. The monthly telephone intervention was provided by the same research nurse where knee pain management advice was offered to the participants. Individuals in the "no intervention" group did not have any contact with the research team between assessments. Outcome measures were assessed at baseline, months 6, 12, 18, 24, and included self reported knee pain (WOMAC), knee specific stiffness (WOMAC), and general physical function (SF-36), psychological score (hospital anxiety and depression scale). At 24 months, the exercise groups were the most successful at reducing pain and demonstrated the largest mean difference in WOMAC knee pain scores -0.82 ($p=0.001$) when compared to non-exercise groups. The exercise groups

demonstrated greater improvements in the stiffness WOMAC index scores with a mean difference of -0.29 (p=0.01) and physical function (SF-36) with a mean difference of -2.57 (p=0.001) when compared to the telephone and no intervention group. The effect of both exercise and telephone contact only demonstrated a significant interaction at 6 months (p=0.001). The mean (SD) (95%CI) bootstrapped total costs of the exercise interventions (exercise and exercise combined with telephone support groups) was £1354 $\pm$ 91 (£1350, £1358) and £1120$\pm$ 84 (£1125, £1132) (p=0.001) for the no exercise interventions (telephone support and no intervention groups). The exercise intervention showed a clinically significant improvement and 50% probability of cost-effectiveness with an ICER of £2570 per patient. It demonstrated to be a cost-effective intervention if payers are willing to spend £8000 per patient for a 50% improvement in knee pain relief.

Thomas et al. (2005) did not pose a well defined question in answerable form. The study examined the combined costs of the two exercise interventions (exercise and exercise with telephone support) and the non-exercise interventions (telephone support and "no intervention") while failing to provide costs of each individual intervention group. The author's presented the data from a patient and health provider perspective (UK's NHS). Although the telephone support intervention and "no intervention" were properly described, the authors failed to provide a thorough description of what type of aerobic and resistance exercises were used in the exercise intervention. The evidence of the programmes' effectiveness appeared to be strong and showed statistical significance among most outcomes. The costs covered both patient and health provider viewpoints, but the authors decided to combine the costs of the two exercise interventions and the two non-exercise interventions. Both capital costs and operating costs were included in the

analysis. The costs appeared to be measured accurately in appropriate physical units although how these units were obtained is poorly reported. Indirect costs were not included as the authors believed it did not carry any weight in the analysis. The costs in the analysis represented total medical costs incurred and not knee-specific costs. In the primary analysis, the authors did not attach a monetary value to the time spent in therapy (personal costs incurred as a result of the study interventions), but provided estimates in the sensitivity analysis. The cost sources were clearly identified though appeared old, relating to nine years prior to publication (Personal Social Services Research Unit, local hospital finance department, 1996 British National Formulary) (87). Costs which occurred during the second year were discounted at 5%. Justification for this discount rate was not given. An incremental cost-effectiveness analysis was performed comparing the costs and consequences of the exercise interventions to the non-exercise interventions. A sensitivity analysis using estimates of personal time (intervention implementation costs) reduced the ICER to £2090 while another sensitivity analysis which only analyzed individuals who presented to their general practitioner for knee pain six months prior to the study demonstrated an ICER of £814. The conclusions of the analyses were based on the ICER results and willingness to pay values. The results were compared to Sevick et al. (2000) and a study which used an aquatic exercise intervention (88). The study did not discuss the generalizability of the results to other settings and patient groups. The authors concluded that the implementation of exercise therapy can provide significant health benefits to individuals with knee pain but will not necessarily reduce medical resource use.

Table 2.2 Patients, Interventions, and Outcomes in the Included Studies

Study	Perspective	Patients	Intervention	Control intervention	Outcome	Conclusion
Hurley et al., 2007	Health care, Societal	·418 individuals ·Aged 50 years or older, ·Mild, moderate or severe knee pain for greater than 6 months	·1)Individual ESCAPE program ·2)Group ESCAPE program ·12 sessions, 2 x week for 6 wks, 10-15 min advice/coping strategies, 30-40 min aerobic and functional exercise	Usual Primary Care	Physical function (WOMAC), QOL (EQ-5D) at 6 month follow-up	No significant differences in health and social care costs between individual rehabilitation and group rehabilitation but ESCAPE was more likely to be more cost-effective than usual primary care
Jessep et al., 2009	N/A	·64 individuals ·Aged 50 years or older ·Diagnosis of osteoarthritis ·mild, moderate or severe knee pain for greater than 6 months	·ESCAPE program ·10 sessions, 2x week for 5 wks, 30-40 min aerobic and functional exercise	Outpatient physiotherapy	Physical function (WOMAC), QOL (EQ-5D), Health care utilization (CSRI) at 12 month follow-up	Both interventions produced physical and psychosocial benefits. ESCAPE program was more cost-effective.
Richardson et al., 2006 & McCarthy et al. 2004	Health care	·214 individuals ·Aged 50 years or older ·Diagnosed with OA of the knee according to ACR recommendations	Home-based + Class-based exercise program, 8wks ·Home-based exercise program, 2x wk for 45 min, sitting to standing exercises, quadriceps isometric contractions, knee extension and flexion exercises, and thigh, hip and calf stretches ·Class-based	Home-based exercise program only, 8 wks, 2x wk for 45 min, sitting to standing exercises, quadriceps isometric contractions, knee extension and flexion exercises, and thigh, hip and calf stretches	Physical dysfunction (ALF), self-reported knee pain (VAS), physical function (WOMAC, SF-36, EQ-5D) at 1, 6 and 12 month follow-ups.	The home-base and class-based programme is likely to be more cost-effective than the home-based programme alone.

			exercise program, 2 x wk, 45 min, circuit of balance, isometric, weight-bearing and functional exercises			
Sevick et al., 2000	Health care	·439 individuals ·Aged 60 years or older ·Radiographic evidence of knee OA ·Reported pain on most days of the month in at least one knee ·Difficulty performing everyday activities due to knee pain.	·1)Aerobic exercise training, 3 month facility-base, 15 month home based, 3x wk, 1hr sessions, walking at 50-70% max heart rate. ·2)Resistance exercise training, 3 month facility-base, 15 month home based, 3x wk, 1hr sessions, nine exercises (leg extension, leg curl, step up, hell raise, chest fly, upright row, military press, biceps curl, and pelvic tilt)	·Health education intervention ·90 min video, nurse telephone contact	Self-reported disability (investigator-developed questionnaire), physical performance (6-min walk test, timed stair climb/descent, lift & carry task, time require to get in and out of the care) at 6, 12 and 18 month follow-up.	Resistance training is marginally more cost-effective than aerobic exercise in improving physical function
Thomas et al., 2005	Patient & Health care	·786 individuals ·Aged 45 years or older ·Self-reported knee pain.	·1) Exercise therapy, 20-30 min daily for 24 months, quadriceps strengthening using graded elastic bands and aerobic exercises ·2) Monthly telephone support ·3) Exercise therapy + Monthly telephone support	No intervention	Self reported knee pain (WOMAC), knee specific stiffness (WOMAC), and general physical function (SF-36), psychological score (hospital anxiety and depression scale) at 6, 12, 18, 24 month follow-ups	The exercise interventions were cost-effective if payers are willing to spend £8000 per patient for a 50% improvement in knee pain.

2.5 Excluded Studies

Although only five studies met the inclusion criteria, results from other studies provided valuable information. A study by Hopman-Rock et al. (89) implemented a six week self-management program for individuals with OA of the hip and knee which included two hours of health education and physical exercise. The study included 120 patients who were between the ages of 55 to 75 years and had a diagnosis of OA according to the ACR criteria. The participants were assigned to either the self-management program group or a "no intervention" control group. Outcome measures included pain using the Impact of Rheumatic Diseases on General health and Lifestyle (IRGL) index, QOL and self-efficacy using the VAS and health care utilization using a relevant questionnaire. Patients were assessed at pre-test (baseline), post-test and 6 month follow-up. The treatment group demonstrated marginal improvements (mean differences) at post-test in pain (IRGL) 0.4, QOL (VAS) 0.3 and self-efficacy (VAS) 3.8 ($p < 0.05$). Results at six months did not demonstrate any significant improvements for pain, QOL, or self-efficacy. A final lesson learnt from this review is that interventions may reduce the use of other healthcare resources which need to be adequately measured in the study. Health care utilization results revealed a decrease in physiotherapist visits in both groups from 7 to 6.6 visits for the control group and 7 to 2.4 visits for the treatment group (multivariate analysis of variance $F=5.06$, $p=0.01$). Although the authors did not include any costs in the analysis, results from this study demonstrate that the combination of exercise and health education may improve short-term QOL while reducing health care utilization, potentially resulting in a cost-effective treatment when compared to "no intervention".

Segal et al. (90) compared various interventions for OA using an evidence-based priority-setting model. The authors, which included an advisory panel of clinicians, health department officers,

consumers, and consumer organization representatives, performed a literature search of all potential OA interventions, conducted economic evaluations with the use of published evidence of costs and outcomes, and then compared the cost-effectiveness of these interventions. The Health-sector-Wide (HsW) disease based model (91) (92), which compares marginal cost-effectiveness ratios, was used to assess the cost-effectiveness of the included interventions. The included interventions must have provided precise program descriptions and quantitative evidence of effectiveness. The search engines which were used to identify the interventions included: MEDLINE, PubMed and CINAHL and Cochrane Reviews. A total of 19 OA interventions were included: weight loss (93) (94) (95; 96; 97), patient education (98) (99) (100) (84), physiotherapy (knee bracing) (101), exercise/strength training (102) (103) (104) (67), pharmacotherapies (105) (106) (107) (108) (109) (110), and surgery (111) (112). Using the HsW model, the most cost effective interventions were total hip replacement and total knee replacements with estimations of $7500 and $10000 per QALY. The other highly cost-effective interventions included exercise and strength training for knee OA with an estimation of over $5000 per QALY and over $10000 per QALY for knee bracing, and capsaicin or glucosamine use. Results suggest that non-pharmacological interventions may be more cost-effective than pharmacological interventions.

Williamson et al. (113) conducted a study which evaluated the effects of standardized Western acupuncture, physiotherapy interventions, and standard management on pain and functional ability among individuals with severe OA of the knee awaiting knee arthroplasty. The study included 181 participants who had unilateral or bilateral knee pain lasting more than 3 months and were on an arthroplasty waiting list due to OA. The three-arm study included an acupuncture intervention, a physiotherapy intervention which included an exercise circuit of static quadriceps

contractions, straight leg raises, sit to stands, stair climbing, calf stretches, theraband resisted knee extensions, wobble board balance training, and freestanding peddle revolutions, and the control group received an exercise and advice information leaflet. The acupuncture and physiotherapy interventions took place once a week for an hour for six-weeks. Outcome measures included pain [Oxford Knee Score (OKS and VAS)], functional ability (OKS and WOMAC), and anxiety/depression [Hospital Anxiety and Depression score (HAD)] at baseline, 7 and 12 week follow up, and at 3 months post-operation. Results which showed statistical significance were the OKS measurements at the 7-week follow-up. The results favoured the acupuncture group, who had the lowest OKS mean (SD) score of 36.8 (7.2), followed by the physiotherapy group 39.2(8.2), and the control group 40.3(8.48). Although the authors did not collect health resource utilization data or perform a CUA, they presented the estimated costs of each intervention. The estimated cost for the physiotherapy group was £9 per patient and £15 per patient for the acupuncture group. Based on these results, it is difficult to determine an accurate estimate of the cost-effectiveness of the two treatment interventions.

Two systematic reviews assessed the literature of cost-effective OA interventions. Roine et al. (2009) (114) reviewed studies which reported cost-effectiveness of exercise-based interventions in the treatment of various diseases. The literature search was performed using the following databases: MEDLINE, Centre for Research and Dissemination, and Cochrane Library. Results demonstrated that three of eight included OA studies were cost-effective (115) (79) (85), while the effects of exercise interventions in the other four studies were relatively weak compared to their costs (116) (89) (88) (113). In comparison with the systematic review for this thesis, Roine et al. included hip OA studies, aquatic exercise interventions and participants who already received knee arthroplasty.

The second systematic review by Zhang et al. (2010) (117) reviewed the available therapies for the treatment of hip and knee OA from 2006 to 2009. The search was performed using the following databases: MEDLINE, EMBASE, CINAHL, AMED, and the Cochrane Library. The results of this systematic review included three economic evaluations for exercise therapy for OA (80) (118) (115), one which has been included in the systematic review of this thesis (80).

2.6 Lessons Learnt

After reviewing the literature, several lessons were taken away as some of the strengths and weaknesses of each study. These important lessons will be addressed in this thesis.

2.6.1 Lesson #1

Valid measurement tools are essential for providing the most accurate results. Hurley et al. (2007) stated that they were uncertain of the sensitivity of their measurement tool leading to scepticism of the study results. A valid measurement tool is crucial in the research process in order to insure internal validity and ensure precision of study results (119).

2.6.2 Lesson # 2

All study data should be analyzed, including incomplete data. Jessep et al. (2009) omitted incomplete datasets from cost calculations which is not the best practice. When incomplete data are omitted from any analysis, valuable information is lost. Complete case analysis may introduce bias and may potentially lose statistical power (120). As an alternative, an intention-to-treat analysis, a widely recommended approach, can be performed using imputation techniques. (120). Richardson et al. (2006) conducted both a complete case analysis and an imputation analysis to compare the difference of the missing data.

2.6.3 Lesson # 3

It is essential to include multidimensional outcomes in studies. Sevick et al. (2000) included numerous outcome measures, but none which measured QOL which prevented the calculation of QALYs. The inclusion of multiple outcome measures can cover diverse aspects such as QOL, physiologic measures and clinical events (121). Including both QOL measures and health utility resource use in existing studies can allow for economic evaluation analyses.

2.6.4 Lesson #4

Economic evaluation studies need to compare all alternatives by a proper incremental analysis. Sevick et al. (2000) did not compare the aerobic group directly to the resistance group. Based on the lower costs and some improved outcomes of the aerobic exercise intervention, it can be argued that the aerobic group dominated the resistance group, a completely different conclusion that the author's make in the article. Comparing all alternatives using a proper incremental analysis can avoid potential ambiguities.

2.6.5 Lesson #5

When conducting analyses, the researcher needs to baseline adjust utility estimates. The results of the mean EQ-5D scores in the analysis by Richardson et al. (2006) at 12 months was 0.53 for the home-based group and 0.58 for the class-based group. After the scores were baseline adjusted, the difference between the two scores was reduced to 0.023 which highlights its importance.

2.6.5 Lesson #6

A probabilistic analysis is required in order to obtain the true measure of uncertainty. Multiple imputation offers convenience and flexibility when analyzing data sets with missing values (122).Richardson et al. (2006) (79) assumed that missing data were missing at random. Using the SOLAS statistical software and using the propensity score method, five imputed data sets were generated to develop a more complete reflection of uncertainty.

2.6.6 Lesson #7

There is a lack of transferability of cost effectiveness data (75). Researchers should be encouraged to measure health care resource use in their studies. If measured effectively, interventions may reduce health care resource use, proving to be a cost-effective. Hopman-Rock et al (2000) (89) presented health care utilization results, revealing a greater decline in physical therapist visits among the experimental group. Williamson et al. (2007) (113), presented estimated costs of each intervention, but failed to collect health resource utilization data, resulting is a weak cost-utility analysis.

2.7 Discussion

One of the strengths of the included studies, with the exception of Jessep et al.(2009) (6), is the large sample sizes they included. In regards to the study populations that were chosen for the studies, it appears that Thomas et al. included a younger population (45 years or older) and did not require a confirmed diagnosis of knee OA. Similarly, Hurley et al. did not require a confirmed diagnosis of knee OA and included individuals with mild, moderate and severe knee pain. The other three studies appeared to have similar study populations with participants being 50 years of age or older and all requiring a confirmed diagnosis of knee OA. Hurley et al.(2007

(76)), Jessep et al.(2004) (6), and Richardson el al.(2006) (79) /McCarthy et al.(2004) (80) had much shorter intervention periods ranging from five to eight weeks compared to Sevick et al. (2000) (85) and Thomas et al. (2005) (86) who had 18 month and 24 month intervention durations respectively. With the exception of Thomas et al. (2005), all the included studies incorporated a supervised facility-based exercise program into their treatment intervention. Sevick et al. (2000) and Richardson et al. (2006) /McCarthy et al. (2004) included both home-based and facility- based intervention for the treatment groups. The intervention frequency was much more intense in the Thomas et al. (2005) study with participants being expected to participate daily in the intervention compared to the other studies who suggested participating two to three times a week. All five studies used different control interventions (usual primary care, outpatient physiotherapy interventions, health education, home-based exercise and no intervention) making it difficult to compare the results. Four of the five studies (76) (6) (79) (86)used the WOMAC osteoarthritis index to measure either physical function or knee pain/stiffness. The EQ-5D appeared to be the most used index among the included studies for QoL and was incorporated in three studies while the SF-36 was included in only two of the five studies. Sevick et al. (2000) used an investigator developed questionnaire which may pose uncertainty of the validity and reliability of the study results. All three studies which compared aerobic exercise to a non-aerobic exercise control intervention demonstrated improved cost-effectiveness for the aerobic exercise interventions (76) (6) (86). The other two studies demonstrated that resistance training may be marginally more cost-effective than aerobic exercise (85) and that the supplementation of a class-based exercise program to a home-based exercise program is likely more cost effective than a home-based program alone (86). In regards

to the perspective of the analyses, only one of the five studies (86) considered the patient payers' perspective while the rest were focused on societal and health care viewpoints.

In regards to the Drummond et al. (1987) (75) checklist, three of the five studies (76) (85) (79) met all of the criteria and appeared to be sound economic evaluations. The other two included studies (6) (86) only met half of the criteria. (See table 2.1)

2.8 Conclusion

To date, there is still a limited amount of studies which have assessed the cost-effectiveness of exercise interventions for the management of OA of the knee. Results of the studies which have performed a cost-effectiveness analysis varied. In most of the studies, the exercise intervention appeared to be the more cost-effective intervention. In order to provide convincing evidence, further research and more studies need to include high-quality economic evaluations to examine the cost-effectiveness of exercise interventions for OA, and particularly on walking programs for this population.

Chapter III

METHODOLOGY

This chapter describes the methodology used for the economic evaluation as well as the randomized controlled trial (RCT) which is a constituent component of this thesis. The research question and outcomes are identified. The economic evaluation methods consist of measuring intervention costs, the valuation and use of resources, and participants' QOL. The primary analysis discusses how missing values were handled and illustrates the use of multiple linear regression, incremental net benefit (INB), and probabilistic analyses to control for uncertainty and variability.

3.1. Research Question

The research question which the thesis is addressing is:

Is a 12 month structured/supervised community-based aerobic walking program combined with a tailored behavioural intervention cost-effective when assessing outcomes over an 18 month period among individuals with OA of the knee ocompared to a supervised community-based aerobic walking program alone and compared to an unsupervised and self-directed control group at 12, 15 and 18 months?

3.2 Details of the randomized controlled trial

3.2.1 Design

A single blind RCT with a parallel group design was conducted at three walking clubs in the Ottawa area. Using 222 subjects were randomized to one of three intervention groups (Refer to the appendices for detailed methodology).

3.2.2 Participants

Eligible participants must have had a confirmed diagnosis of mild to moderate unilateral or bilateral OA of the knee, reported pain for at least 3 months, were not already engaged in regular PA, were able to ambulate for a minimum of 20 minutes and be available three times a week over an 18-month period. Exclusion criteria comprised of participation in regular PA more than two times per week for over 20 minutes per session during the previous 6 months, severe OA of the knee or weight bearing joints of the lower extremity, no written consent from his/her physician for participation in the study, pain at rest or at night, corticosteroid injections or other rehabilitation treatment during the 12 months prior to the study, uncontrolled hypertension, systolic blood pressure greater than 160 mm Hg, significant cognitive deficit, planned surgery within the 18 months, intention to move away from the Ottawa region within the 18 months, inability to communicate in English or French, and unwilling to give consent. Both the University of Ottawa Research Ethics Board (H 01-07-08) and the City of Ottawa Public health Research Ethics Board (110-06) approved this community-based study. Informed consent was given by all participants.

3.2.3 Walking Interventions

Two-hundred-and-twenty-two subjects were randomized to one of three groups: 1) A walking behavioural group (WB) which received a behavioural intervention in combination with a 12-month supervised community-based aerobic walking program and an educational pamphlet (n-69); 2) A supervised community-based aerobic walking group (W) who only participated the supervised community-based aerobic walking program and received an educational pamphlet (n=79); 3) A control group (C) who participated in an unsupervised self-directed walking program and received an educational pamphlet (n=74). All 3 groups were provided with

pedometers and log books to be completed, recording the number of steps walked and the amount of PA performed. Following randomization, the community-based aerobic walking programs took place at three different walking clubs in the Ottawa region where the program and its progression were explained to each subject in the WB and W groups. Both supervised walking group interventions (WB and W) included three weekly scheduled sessions which included a 10 minute warm-up of light exercises, 45 minutes of aerobic walking, and then followed by a 10 minute cool-down of light exercises and stretching. The recommended maximum heart rate during the walking portion of the intervention ranged from 50%-70% (46) (47) (48)(Appendix 3.1). Subjects in the WB group participated in the *Program for Arthritis Control through Education and Exercise* (PACEex) (123) program which consisted of 20 two-hour group sessions consisting of short term goals setting and education regarding the benefits of PA including walking. In addition, participants took part in monthly individual sessions in which long-term goals and potential barriers with adhering to the program were discussed. Individuals in the self-directed walking group (C) were encouraged to consult an educational pamphlet on walking and OA, complete a log book which recorded his/her daily step count using a pedometer and the number of walking sessions he/she participated in. The log books were used to measure PA and compliance to the walking programs. These individuals had no contact with subjects from the other groups. We hypothesized that the WB intervention would be most cost-effective compared to the W and C interventions.

3.2.4 Clinical Trial Outcomes

The a priori primary outcome measures was QOL using the Short-Form 36 Health Survey (SF-36) (124) and the Arthritis Impact Measurement Scales 2 (AIMS-2) (125). Other outcome

measures included change in PA level using the 7-day Physical Activity Recall (PAR), self-efficacy using the Stanford Self-Efficacy Questionnaire (126) and health resource utilization using a related questionnaire (127). Measurements were conducted by a blinded evaluator every three months over the course of the 12-month intervention period (i.e. at baseline, 3, 6, 9, 12 months) and follow-up measurements were conducted at 15 and 18 months (3 and 6 months post-intervention)**.** A respondent who has completed the SF-36 can produce an estimate of a preference based single index measure for health through the use of the SF-6D which allowed for the calculation of QALYs.

3.3 Methodology for the Economic Evaluation

3.3.1 Perspective

The study was conducted from both the payer (Ministry of Health) and the societal perspective.

3.3.2 Interventions

Three walking interventions were assessed: 1) a 12-month supervised community-based aerobic walking program supplemented with the PACEex educational program and an educational pamphlet (WB); 2) a 12-month supervised community-based aerobic walking program supplemented with an educational pamphlet; 3) an educational pamphlet on walking and OA (C) (See Section 3.2.3)

3.3.3 Form of Analysis, Time Horizon and Discounting

The cost-utility analysis measured the differences in QALYs based on utility values from the SF-36 and total costs between each of the three intervention groups at 12, 15, and 18- month follow-ups. The analysis consisted of calculating the INB and cost-effectiveness acceptability curves

(CEACs) using cost and QALY data. With a short assessment period of 18 months, discounting costs was unnecessary. All costs were calculated and are presented in 2010 Canadian dollars.

3.3.4 Intervention Costs

The interventions costs are presented as total costs and costs per patient (Table 3.1). Both the W and WB interventions shared physical and human resources as well as the equipment of the walking clubs. The two interventions groups required sphygmomanometers and heart rate monitors for each participant. In addition, participants in these groups were reimbursed for walking club membership fees. The W and WB groups required exercise therapists to monitor participants and record measurements. The costs of the exercise therapists were based on annual salaries. An exercise therapist was present where he/she monitored and measured participants for three hours per session, three times a week. The walking club at one location operated for approximately three years, while the other two only operated for approximately one year and six months. Exercise therapists were not paid during the follow-up phase (between 12 to 18 months). Exercise therapist costs were then calculated as follows:

Total exercise therapist cost= (3 years x annual exercise therapist salary) + (1.5 years x annual exercise therapist salary) + (1.5 years x annual exercise therapist salary)

The WB group required additional resources due to the addition of the PACE-Ex program. Additional costs included binders for each participant, the instructor's laptop, and the instructor's salary. All three groups were provided with pedometers, logbooks and pamphlets. No costs were associated with the pamphlets as they were provided free of charge by the City of Ottawa Department of Public Health and were given to all participants (i.e. the incremental cost was zero).

Table 3.1Intervention costs

W (n=79)				WB (n=69)				C (n=74)			
	Quantity	Total($)	Per participant ($)		Quantity	Total($)	Per participant ($)		Quantity	Total($)	Per participant ($)
Sphygmo-manometer	3	$78.63	$0.53	Sphygmo-manometer	3	$78.63	0.53	Pedometers	74	$2,134.90	$28.85
Heart rate monitors	79	$12,872.86	$162.94	Heart rate monitors	69	$11,242.86	162.94	Logbooks	74	$444.00	$6.00
Pedometers	79	$2,279.15	$28.85	Pedometers	69	$1,990.65	28.85	Pamphlets	74	$0.00	$0.00
Logbooks	79	$474.00	$6.00	Logbooks	69	$414.00	6.00				
Pamphlets	79	$0.00	$0.00	Pamphlets	69	$0.00	$0.00				
Walking club membership	79	$790.00	$10.00	Walking club membership	69	$690	$10.00				
Exercise Therapists*	3	$16,848.00	$208.70	Exercise Therapists*	3	$16,848.00	$208.70				
				PACE-Ex program							
				Binders	69	$382.95	$5.55				
				Instructor**	1	$1,0350	$150.00				
				Laptop	1	$597.77	$8.66				
Total Cost ($)		$**33,342.64**	$**417.02**			$**42,594.86**	$**581.24**			$**2,578.90**	$**34.85**

*Exercise therapists earned $12.00 per hour

**PACE-EX instructor earned $25.00 per hour

3.3.5 Measurement of Resource use

Resource use data were collected retrospectively at baseline and at each follow-up assessment (months 3, 6, 9, 12, 15, 18) using a health resource utilization questionnaire. The data were collected face-to-face by the evaluator. The health resource utilization questionnaire included information asking participants how often in the last three months they had visited health professionals, such general practitioners, orthopaedic surgeons or allied health professionals. They were also asked how often they visited the emergency department of a hospital, if and how many nights they had been admitted overnight at a hospital, if they had underwent diagnostics tests and procedures including blood tests, how many prescription medications were taken, and if they had missed a full day of paid work because of an illness (127) (Appendix 3.2).

The health resource utilization questionnaire used in the RCT was not specific to OA. In order to narrow down the questions and apply OA specific health resources, a rheumatologist (PT) was consulted. General questions which required specification included “how often the participant visited a physician specialist or allied health professional”, “how often a participant had diagnostic or blood tests performed” and “how many different prescription drugs the participants was taking at that moment”. The rheumatologist identified orthopaedic surgeons to be the most relevant physician specialist and physiotherapists as the most relevant allied health professionals for OA patients. Participants in the study were asked to identify which medications they were taking during the admission process of the study. With the assistance of the rheumatologist, a list of the top 24 most frequently used medications most relevant to OA patients was developed and costed.

The friction cost method to measuring the cost of lost productivity was adopted. This limits lost productivity to the period time for which it would take to replace a worker. Based on information collected within the RCT, the number of lost work days was imputed as a "zero" if the participant stated that he or she was retired. In addition, to the number of lost work days was restricted to 10 days over a 3 month period, reflective of the average time to replace a worker.

3.3.6 Valuation of resources

Unit costs were estimated from a patient payer's and a societal perspective (Table 3.2). Resource use data were multiplied to the respective unit costs. Unit costs were obtained from the schedule of fees from the Ontario Ministry of Health and Long-Term Care (128), Ontario Ministry's Schedule of Benefits for Laboratory Services (129), Ontario Case Costing Initiative (130), Statistics Canada (131) and an Ontario costing report (132). With a short assessment period of 18 months, discounting costs was unnecessary. All costs were calculated and are presented in 2010 Canadian dollars.

General practitioner and orthopedic surgeon fees were costed according to the number of patient consultations (128) while physiotherapists and occupational therapists were priced according to their mean hourly fee (132). The duration of an average session with either a physiotherapist or occupational therapist has been estimated to be approximately thirty minutes (132). Knee x-ray diagnostic tests (128) and blood tests (129) were costed for each performed test. The cost of an overnight admission at a hospital was estimated using a costing analysis tool based on collection of case costing data from numerous local health integration networks (LHIN) across Ontario (130). The cost of one night average was estimated based on data from patients who were

categorized as having arthritis and were between the ages of 18 to 69 years old. Visits to the hospital emergency department were calculated per consultation (128). With the list of frequently used medications among study participants, a daily drug cost average was calculated using prices from the Ontario Drug Benefit Formulary (133). Lastly, loss of productivity costs was calculated using the most up-to-date (2009) available Census data from Statistics Canada. Given the average personal annual income in Ontario (2009) (131), the mean hourly wage was estimated. A missed full day of paid work was then calculated as 7.5 hours of lost wages.

Table 3.2 Unit Costs for Ontario (2010 Canadian Dollars)

Cost Variable	Unit Cost*	Reference
General Practitioner		Ontario Ministry
First consultation	$67.50	of Health and
Second consultation	$42.35	Long-Term Care
Third or more	$30.10	
Physician Specialist (Orthopedic Surgeon)		Ontario Ministry
First consultation	$78.00	of Health and
Second consultation	$45.85	Long-Term Care
Third or more	$30.10	
Allied Health professionals		Long Term Care in
Physiotherapist (0.5 hours)	$52.20	Ontario – 2010 [1]
Occupational therapist (0.5 hours)	$50.00	
Diagnostic tests		
Knee (including patella) X-Ray (two views)	$22.05	Ontario Ministry of Health and Long-Term Care
Laboratory tests		
Blood test (complete blood count)	$16.03	Ontario Ministry's Schedule of Benefits for Laboratory Services
Overnight Hospital Admission		
One Night Average (Arthritis Grouper, Ages 18-69)	$925.42	Ontario Case Costing Initiative
Hospital Emergency Department Visits consultation	$76.90	Ontario Ministry of Health and Long-Term Care
Prescription Drugs (daily average per drug)	$0.62	Ontario Ministry of Health and Long-Term Care
Loss of Productivity		Statistics Canada
Missed full day of paid work (7.5hours)	$176.48	

*All costs are reported in 2010 Canadian dollars

[1] https://hermes.manulife.com/canada/repsrcfm-dir.nsf/Public/ThecostoflongtermcareinOntario/$File/ONTARIO_LTC_CostReport.pdf

3.3.7 Calculation of Quality Adjusted Life Years (QALYs)

Utility values were calculated for each three month period of the trial using data from the SF-36 questionnaires collected as part of the RCT. The SF-36 health survey is a standardized questionnaire which consists of eight patient health dimensions which assesses the perception of patients' health (124). Respondents are presented with different choices of responses that are numerically coded which are summed to produce a raw dimension score. Utility values were determined through a method used by Brazier et al. (134). The SF-36 data were converted into the Short Form Six-Dimension utility index (SF-6D) classification in order to generate preference scores. The SF-6D, a generic preference-based single index measure of health, uses the SF-36 items to generate QALYs (134). It is composed of a scoring table, six multi-level dimensions (physical functioning, role limitations, social functioning, pain, mental health, and vitality), and can describe 18,000 different health states (135). The scoring table is used to calculate utility values, between 0 (dead) and healthy (1.0). The different dimensions contain different classification levels. The dimensions "physical functioning" and "pain" have 6 levels, "social functioning", "mental health" and "vitality" have 5 levels and "role limitations" has 4 levels. The index is calculated by adding the negative values to a constant of 1 (perfect health state). The analysis used revised weights derived using a set of non-parametric Bayesian preference weights (136) (137).

The changes in utility scores were estimated for each patient over each time period. QALYs were estimated by applying the changed scores to the mean baseline utility for all participants. Adjusting for baseline utility is standard methodology as baseline utility is highly correlated with

QALYs over the study duration, furthermore unaccounted imbalances in baseline utility when measuring QALY differences often leads to inaccurate cost-effectiveness results (138).

3.4 Primary analysis

The primary analysis compared the INB of the walking intervention and the combined walking and behavioural intervention, to the self-directed control group. The mean and standard errors for the costs (total and by category) and change in utility scores were estimated for each time period by treatment. All analyses were performed using SPSS Statistics 17.0. The analysis was performed from both a societal and health care payer's perspective.

3.4.1 Handling Missing Data

Missing data can be a potentially immense limitation in a cost-effectiveness analysis, affecting the validity of study results if an appropriate strategy is not considered (139). A complete-case analysis was first conducted to determine the influence of missing data. Missing data can be referred to as missing at random (MAR), missing completely at random (MCAR) or missing not at random (MNAR).

To assist in classification, missing data were first categorized as missing due to a drop-out and missing due to a missed follow-up evaluation. The frequency of missing values and unanswered questions were analyzed to determine if there were any patterns. This was accomplished by first measuring the number of participants who completed each assessment, followed by analyzing the number of missing items per participant at each assessment point.

Data are considered to be MCAR when the probability of a missing observation is completely unrelated to any variables, and is classified as MAR when a missing observation is independent of a value of interest after controlling for a separate variable (140). For MAR and MCAR, health resource utilization (HRU) missing data produced by missed follow-up evaluations was assumed to be MAR. Thus, to handle such missing data, the appropriate technique of multiple imputation was adopted. Multiple imputation is a process which generates imputed values based on the existing data (141). An error component is added to the predicted values in order to estimate what the missing values would be (142). Imputations are repeated several times to correct for the underestimation of standard errors. In this study, pooled results were taken from five created imputed datasets. Pooled mean and standard errors (SE) were calculated for each health care resource cost.

Missing data due to drop-outs with given reasons cannot be considered MAR or MCAR and must be considered MNAR. For such data, the multiple imputation technique was not used for this type of missing data as it is not acceptable practice when patient specific reasons are given (143). With such data, it is necessary to make assumptions around the projected resource use. In this instance, it was assumed that the effect of treatment on resource use would end once the patient dropped out. Thus, health resource utilization (HRU) missing data produced by drop outs were imputed with baseline data. Missing utility data (SF-36) were imputed using the last value carried forward technique.

Although the main method of analysis consisted of using multiple imputation, separate analyses were performed to assess and compare the influence of missing data. Analyses which excluded

data from drop-outs (missing values imputed with baseline data), data from participants who missed follow-up evaluations (missing values imputed using multiple imputation), and incomplete data were conducted.

3.4.2 City of Ottawa Bus Strike

There was uncertainty over whether participants had missed an evaluation due to a bus strike (Table 3.3). The majority of participants relied on public transportation to access the shopping malls where the study took place. From December 10, 2008 to February 9, 2009, City of Ottawa employees working for "O.C Transpo" halted all transportation services. Furthermore, the strike was declared over on February 10, 2009, yet full services were not restored until April 6, 2009. The number of participants who had dropped out or who had missed a follow-up evaluation during these time periods were calculated in order to conclude the effect of the bus strike on missing data. It was eventually concluded that the bus strike had no major impact on missing data.

Table 3.3 Missed evaluations during the OC Transpo Bus Strike

December 10, 2008 – February 9, 2009							
	3 months	**6 months**	**9 months**	**12 months**	**15 months**	**18 moths**	**Total**
Drop-out	3	10	1	9	3	3	29
No- Show	0	1	1	0	2	0	4
February 10, 2009 – April 6, 2009							
	3 months	6 months	9 months	12 months	15 months	18 moths	Total
Drop-out	3	5	17	2	1	1	29
No-Show	0	1	0	1	0	0	2

3.4.3Multiple Linear Regression Analyses to Handle Uncertainty and Variability

A multiple linear regression analysis is a statistical technique which allows one to investigate the linear relationship between a predictor and criterion variables (144). Multiple linear regression analyses were performed to handle differences in the patient sample as well as to allow for a sub-group analysis. Nine separate multiple linear regression analyses were performed to determine the effect of covariates on total societal costs, total health care costs, and QALYs at 12, 15, and 18 months. Variables that were tested and thought to have a potential influence on the respective outcome included: age (years), the duration of OA (years), gender, level of education (college/ university), obesity (BMI of 30kg/m^2 or greater), and level of intensity [total metabolic equivalent of task (MET) score]. Baseline costs were included in the cost regression models. Baseline utility values were included in the QALY regression models. Dummy variables were created for the walking (W) and walking behavioural (WB) interventions.

There appears to be controversy regarding the selection of regression model. Including too many irrelevant explanatory variables using a simultaneous model can increase variation of the parameters, leading to inaccurate estimates and potential confounding (144). On the other hand, hierarchical models, such as a stepwise model, are not always preferred as they are not guided by theory, and rely on set orders of entry/removal without considering logical or causal relevance prior to the analysis (145). For this study, both a simultaneous model including all clinically meaningful covariates, and a stepwise model, including only significant covariates were used.

3.4.3.1 Analyses including all covariates

This analysis includes all variables which are pre-specified as clinically important and may impact costs and/or QALYs. Within SPSS, these regression analyses used the "Enter" simultaneous method which enters all variables into the analysis in a single step. All covariates were treated equally and simultaneously, as none of the variables were considered to be superior to any other. For interpretation, variables were assumed to be significant if $p \leq 0.2$.

3.4.3.2 Multiple Linear regression analyses using "stepwise" method

Using the "stepwise" method, covariates were entered and removed in the equation at different stages based on predefined criteria. During each step, the covariate with the smallest probability of "*f*"(≤ 0.05) was entered in the equation, while the covariates already in the equation with a sufficiently large "*f*"(≥ 0.2) were removed. This process continued until covariates were no longer eligible for entry/removal in the equation.

3.4.4. Incremental Net Benefit Analysis (INB)

The nature of ratio statistics such as incremental cost-effectiveness ratios (ICERs) preclude the use of advanced statistical techniques to handle uncertainty (146). Thus analysis used the INB framework to explore inferences. The INB analysis is defined as the incremental utility value (QALY) multiplied by the willingness to pay threshold (WTP), less the incremental costs:

$$\mathbf{INB} = \Delta_{\mathbf{QALY}} \times \lambda - \Delta_{\mathbf{Cost}}$$

WTP, often denoted as λ, is the value that policy makers are willing to pay for a unit of effectiveness (146). The INB analyses were performed at 12, 15 and 18 months for both societal and health care costs with WTPs of $50, 000.00 per QALY, which is commonly used in cost-effectiveness analyses as recommended by the Ontario Ministry of Health and Long-Term Care to indicate good value for money (147). Furthermore, WTPs of $0.00 per QALY and increments of $10, 000.00 up to $100,000.00 per QALY were analyzed through the use of multiple linear regression analyses using the simultaneous method.

3.4.5 Probabilistic Analyses

3.4.5.1 Cost-Effectiveness Acceptability Curves

Cost-effective acceptability curves (CEACs) have been argued to be an appropriate approach to present uncertainty about the incremental cost effectiveness of interventions (148). CEACs plot the probability of each intervention being cost-effective in reference to a decision-makers' defined maximum willingness to pay threshold (WTP) (149) and allow cost-effectiveness uncertainty information to be summarized graphically (150).

A probability uncertainty analysis was performed using the method of Monte Carlo simulation. Monte Carlo simulations allow uncertain random variables to be quantitatively fitted in a model (151). Cost and QALY estimates associated with the three interventions were obtained by running the model with 5000 repetitions, using a random sample of values. The simulation then allowed for the calculation of mean cost-effectiveness probabilities for each WTP increment ($0 to $100,000 per QALY). CEACs for both health care costs and societal costs were then plotted for each time period (12, 15 and 18 months).

3.4.5.3 Expected Value of Perfect Information Analysis

Howard (1966) (152) defines the expected value of perfect information (EVPI) as the "expected value of obtaining perfect knowledge of the true values of all parameters". An EVPI analysis places a monetary value on the potential for further research by eliminating parameter uncertainty (153). The EVPI in this case is the maximum a decision maker is willing to spend to reduce the uncertainty and acquire additional evidence on supervised aerobic walking programs for future decisions.

EVPI is calculated as the expected value of having perfect information less the expected value of current information:

$$EVPI = E_{\theta} \max_{\alpha} \beta_{\alpha}(\theta,\lambda) - \max_{\alpha} E_{\theta}\, \beta_{\alpha}(\theta,\lambda)$$

Where β_{α} represents the monetary net benefit of implementing a supervised aerobic walking program, which is the function of uncertain parameters θ, and the maximum willing to pay threshold λ (154).

If the EVPI exceeded the expected costs (willingness to pay threshold) of additional research, then it was deemed to be potentially cost-effective to pursue further research.

EVPI's were estimated for WTPs of \$0.00 per QALY and increments of \$10, 000.00 up to \$100,000.00 per QALY through the use of the INB distributions from the multiple linear regression analyses. This was repeated 5000 times in order to obtain a mean EVPI estimate for each WTP value.

3.4.6 Sensitivity analysis

Subgroup analysis was conducted based on the following patient characteristics: age, gender, duration of OA, obesity (body mass index > 30kg/m^2), and education (a minimum education of "some college or more"). This was conducted through linear regression on INB including all covariates and dummy variables for participants in the W and WB groups as independent variables. Base analysis was conducted from the health care system perspective at 18 months.

Chapter IV

RESULTS

The following chapter provides the results from the RCT and the methodology used for the cost-utility analysis. Participant characteristics, QALYs, health care resource use, and total intervention costs are presented using both adjusted and unadjusted estimates. Total costs are demonstrated from the health care payer's and societal perspectives. Estimates were calculated using multiple linear regression analyses using both simultaneous and hierarchical models. In addition, alternate estimates are given using separate analyses which excluded incomplete cases, drop-outs, and imputations. The cost-effectiveness of each intervention is illustrated through the use of an incremental net benefit (INB) analysis, cost-effectiveness acceptability curves (CEACs), and expected value of perfect information (EVPI) analysis. A sensitivity analysis is presented focussing on particular subgroups.

4.1 Participant characteristics

A total of 222 individuals (153 women) were recruited (Table 4.1). The baseline mean ($\pm$SD) age was 63 years ($\pm$8.6), mean weight 82.2kg ($\pm$16.6), mean body mass index (BMI) 29.8 kg/m^2 ($\pm$5.4), and mean duration of OA was 10.3 years ($\pm$9.3). The majority of participants (40.1%) were affected by OA in the right knee. Only 13.1% of participants required a walking aid. The majority of participants were Caucasian (88.7%), were married (56.8%), and were college graduates (29.3%). There were no statistically significant differences between groups at baseline for the economical outcomes of interest in this thesis.

Non-statistically significant differences between in-group comparisons revealed that the self-directed walking group (C) was predominately affected with OA in the left knee (37.8%) while both the walking group (W) (41.8%) and the walking and behavioural group (WB) (44.9%) were

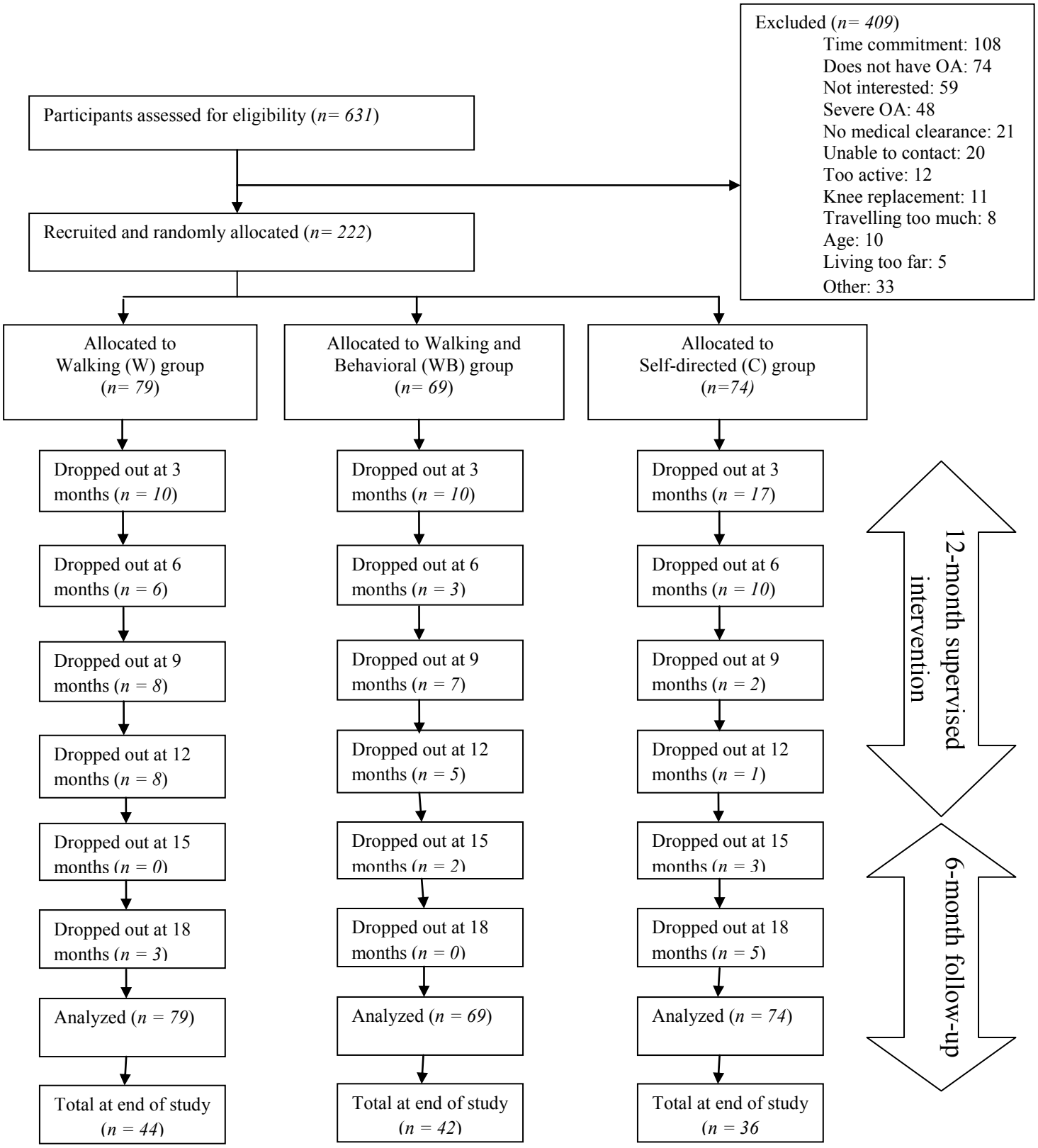
mostly affected in the right knee. The W (31.6%) and WB (30.4%) groups appeared to have a slightly higher level of education as the majority of participants in these groups were college graduates while the majority in the self-directed group (C) only completed 1 to 4 years of college (29.7%). The WB group had a higher mean duration of OA (11.3 years) compared to the W group (9.54 years) and the C group (10.0 years). The WB group had the highest mean BMI (30.3kg/m^2) compared to the W group (29.4 kg/m^2) and the C group (29.9 kg/m^2).

A total of 44 of the 79 participants in the W group, 42 of the 69 in the WB group and 36 of the 74 participants in the self-directed group (C) completed the study. A total of 100 participants dropped out of the study for various reasons (Figure 4.1).

Table 4.1 Participant Characteristics

Characteristic	Walking (n=79)	Walking and Behavioural (n=69)	Self-Directed (n=74)	Total
Mean age (SD), yrs	63.9 (10.3)	63.9 (8.2)	62.3(6.8)	63.4 (8.6)
Missing Data	*0*	*0*	*0*	*0*
Men/women, (%)	24 (30.4) / 55 (69.9)	18 (26.1) / 51 (73.9)	27 (36.5) / 47 (63.5)	69 (31.1) / 153 (68.9)
Missing Data	*0*	*0*	*0*	*0*
Affected knee, n (%)				
Right	33 (41.8)	31 (44.9)	25 (33.8)	89 (40.1)
Left	31(39.2)	23 (33.3)	28 (37.8)	82 (36.9)
Both side	15 (19.0)	15 (28.4)	21 (28.4)	51 (23.0)
Missing Data	*0*	*0*	*0*	*0*
Mean duration of OA (SD), yrs	9.54 (8.09)	11.3 (9.7)	10.0 (9.9)	10.3 (9.3)
Missing Data	*0*	*0*	*0*	*0*
Mean weight (SD), kg	80.7 (18.5)	83.1 (15.4)	83.0(15.8)	82.2 (16.6)
Missing Data	*0*	*1*	*0*	*0*
Mean BMI (SD), kg/m^2	29.4 (5.4)	30.3 (5.6)	29.9(5.3)	29.8 (5.4)
Missing Data	*0*	*2*	*4*	*6*
Walking aid, n (%)				
Yes	10 (12.7)	10 (14.5)	9 (12.2)	29 (13.1)
No	69 (87.3)	58 (84.1)	64 (86.5)	191 (86.0)
Missing Data	*0*	*1*	*1*	*2*
Racial background, n (%)				
White	69 (87.3)	60 (87.0)	68 (91.9)	197 (88.7)
Black	1 (1.3)	3 (4.3)	1 (1.4)	5 (2.3)
Hispanic	2 (2.5)	2 (2.9)	4 (5.4)	8 (3.6)
Asian or Pacific Islander	5 (6.3)	4 (5.8)	1 (1.4)	10 (4.5)
American Indian or Alaskan native	1 (1.3)	0 (0)	0 (0)	1 (0.5)
Other	1 (1.3)	0 (0)	0 (0)	1 (0.5)
Missing Data	*0*	*0*	*0*	*0*
Marital status, n (%)				
Married	46 (58.2)	36 (52.2)	44 (59.5)	126 (56.8)
Separated	2 (2.5)	1 (1.4)	1 (1.4)	4 (1.8)
Divorced	9 (11.4)	17 (24.6)	8 (10.8)	34 (15.3)
Widowed	17 (21.5)	11 (15.9)	9 (12.2)	37 (16.7)
Never Married	5 (6.3)	4 (5.8)	12 (16.2)	21 (9.5)
Missing Data	*0*	*0*	*0*	*0*
Level of education, n (%)				
Less than 7 yrs of school	2 (2.5)	1 (1.4)	1 (1.4)	4 (1.8)
Grades 7 through 9	5 (6.3)	0 (0)	0 (0)	5 (2.3)
Grades 10 through 11	7 (8.9)	4 (5.8)	5 (6.8)	16 (7.2)
High school graduate	13 (16.5)	16 (23.2)	8 (10.8)	37 (16.7)
1 to 4 yrs of college	13 (16.5)	9 (13.0)	22 (29.7)	44 (19.8)
College graduate	25 (31.6)	21 (30.4)	19 (25.7)	65 (29.3)
Professional or Graduate school	14 (17.7)	18 (26.1)	19 (25.7)	51 (23.0)
Missing Data	*0*	*0*	*0*	*0*

Figure 4.1 Study Flow Chart



4.2 Outcomes

4.2.1. Utility values and QALYs

Non-baseline adjusted mean QALY scores over 18 months among the W group were of 0.99 (±0.01), 1.03 (±0.01) for the WB group, and 1.05(±0.02) for the self-directed group (C). Baseline utility scores did not appear to be balanced among the three groups: 0.67 for the W group, 0.66 for the WB group, and 0.69 for the self-directed (C) group. At 18-months follow-up, the difference in mean utility values when compared to baseline for the W group was 0 (±0.10). Among the WB group, mean utility decreased by 0.04 (±0.10) and increased by 0.01 (±0.07) for the self-directed group. Similar results were seen at 12 and 15 months (Appendix 4.1). After adjusting for baseline utility, the QALY scores for 18 months were equivalent among the W and WB groups with mean (±SE) QALYs of 1.01 (±0.02). The mean baseline adjusted QALY of the self-directed group was 1.05(±0.02) over 18 months (Table 4.2).

4.2.2. Resource Use

4.2.2. 1.Mean Costs

Over 18 months, the WB group demonstrated the highest mean (±SE) general physician costs $93.65 (±8.64) compared to the W group $88.39 (±7.46) and self-directed group (C) $84.02 (±9.46). Physician specialist costs were highest among the WB group $81.45 (±9.29) compared to the W group $74.27 (±7.94) and self-directed group (C) $71.01 (±8.83). The W group exhibited the highest mean allied professional costs $329.92 (±47.98) compared to the WB group $253 (±49.40) and self-directed group (C) $254 (±36.32). The W group also had the highest mean diagnostic test costs $23.53(±4.02) compared to the WB group $17.15 (±2.57) and self-directed group (C) $16.40 (±2.62). The highest laboratory test costs were seen among the WB

group $20.98 (±2.55) compared to $19.49 (±3.21) for the W group and $20.45 (±3.67) for the self-directed group (C). The self-directed group (C) had the highest mean overnight admission hospital costs $109.29 (±21.69) compared to the W group $104.65 (±24.22) and WB group $81.70 (±24.74). The self-directed group (C) visited the hospital emergency department most often with a mean cost of $25.25 (±6.80) while the W group paid $24.46 (±5.85) and the WB group paid $22.71 (±5.65). The WB group paid the most for daily medication costs $2.04 (±0.19) while the W group paid $2.00 (±0.15) and the self-directed group (C) paid $1.91 (±0.18). The highest mean loss of productivity costs were demonstrated by the WB group$25.32 (±25.32) followed by $14.24 (±12.08) for the self-directed group (C). There was no loss of productivity costs among the W group (Appendix 4.1).

The major differences when compared to 12 months were that the W group had the highest general physician costs $77.66 (±6.87), laboratory test costs $14.89 (±1.97), overnight admission hospital costs $204.95 (±45.86), hospital emergency department costs $23.17 (±4.44) and loss of productivity costs $33.44 (±23.99). The self-directed group (C) paid the most for physician specialist costs $70.33 (±8.74) (Appendix 4.1).

When compared to 15 months, the only differences were that the W group paid the most for physician specialist costs $78.59 (±7.00), laboratory test costs $20.11 (±2.95), overnight admission hospital costs $222.20 (±82.19), and daily medication costs $1.93 (±0.10). The self-directed group (C) demonstrated the highest hospital emergency department costs $26.52 (±5.67) and greatest loss of productivity costs $59.31 (±32.62) (Appendix 4.1).

4.2.2. 2. Differences in total mean costs

At 18 months, when compared to the self-directed group (C) , the W group demonstrated less mean total general physician costs (-$2.17), total overnight admission hospital costs (-$4.95), total hospital emergency department costs ($4.18), and fewer loss of productivity costs (-$179.28). The WB group, when compared to the self-directed group (C) paid less mean total allied health professional costs (-$161.77), total overnight admission hospital costs (-$298.17), total hospital emergency department costs (-$37.44), and fewer loss of productivity costs (-$324.18) (Table 4.2).

4.3 Intervention Costs

The combined 12-month supervised community-based walking program and behavioural intervention (WB group) was the most expensive intervention with a cost of $581.24 per participant. The cost of the 12-month supervised community-based walking program (W group) was $412.02 per participant while the cost of the self-directed intervention was only $34.85 per participant (Table 3.2).

Table 4.2 Costs (Canadian $) and QALYs

	Walking (n=79)		Walking + Behavioural (n=69)		Self-directed (n=74)		Walking vs. Self-directed (difference)	Walking Behavioural vs. Self-directed (difference)
Intervention costs	$417.02	-	$581.24	-	$34.85	-	$382.17	$546.39
General Physician costs	$469.06	($30.27)	$483.70	($35.73)	$471.23	($38.51)	$-2.17	$12.47
Physician Specialist costs	$408.37	($36.06)	$423.26	($45.19)	$394.24	($40.96)	$14.13	$29.01
Allied Health Professional costs	$1,768.23	($236.98)	$1301.14	($168.97)	$1462.91	($210.40)	$305.32	$-161.77
Diagnostic Test costs	$128.13	($10.40)	$118.94	($13.04)	$109.48	($12.34)	$18.65	$9.46
Laboratory Test costs	$92.05	($8.75)	$100.85	($10.12)	$91.25	($9.11)	$0.80	$9.60
Overnight Admission Hospital costs	$728.70	($139.65)	$435.48	($72.22)	$733.65	($144.75)	$-4.95	$-298.17
Hospital Emergency Department costs	$108.48	($14.66)	$75.22	($12.82)	$112.66	($15.54)	$-4.18	$-37.44
Medication costs (daily)	$11.44	($0.79)	$11.92	($1.03)	$11.18	($1.16)	$0.25	$0.73
Loss of productivity costs	$195.62	($59.32)	$50.72	($30.88)	$374.90	($102.86)	$-179.28	$-324.18
Total Health care costs	$3,721.73	($278.60)	$3,269.52	($233.10)	$3,085.77	($290.69)	$635.96	$183.75
Total Societal Costs	$3,922.44	($301.51)	$3,320.24	($236.50)	$3,471.08	($300.80)	$451.36	$-150.84
QALYs (baseline adjusted)	1.01	(0.02)	1.01	(0.02)	1.05	(0.02)	-0.04	-0.04
QALYs (non-baseline adjusted)	0.99	(0.01)	1.03	(0.01)	1.04	(0.02)	-0.05	-0.01

Mean (SE)

4.4 Cost-Effectiveness

4.4.1 Unadjusted estimates

Total health care costs were summarized as the combined total of intervention costs and resource costs, excluding loss of productivity costs. At 18-months, the W group incurred the highest mean total health care costs (±SE) $3721.73 (±278.60), while the WB group had a mean health care total cost of $3269.52 (±233.10). The self-directed group (C) had a mean total cost of $3085.77 (±290.69) (Tables 4.2 & 4.3). Similar results were seen at 12 months and 15 months (Table 4.3).

Total societal costs were summarized as the combined total of intervention costs, health care costs, and loss of productivity costs. Again, the W group demonstrated the highest mean total societal costs (±SE) at 18-months $3922.44 (±301.51), while the WB group had a mean total societal cost of $3320.24 (±236.50) at 18 months. The self-directed group (C) had a mean total cost of $3471.08 (±300.80) (Table 4.2 & 4.4). Results at 12 and 15 months were analogous (Table 4.4).

Mean (±SE) baseline adjusted QALY scores at 18 months were 1.01 (±0.02) among the W and WB groups and 1.05(±0.02) among the self-directed group (C) .

Table 4.3 Cumulative Total Health care costs and QALYs at each time period

	Walking				Walking + Behavioural				Self-directed			
	Total Costs ($)		QALYs*		Total Costs($)		QALYs*		Total Costs($)		QALYs*	
3 months	$785.27	($51.40)	0.17	(0.00)	$911.98	($47.41)	0.17	(0.00)	$380.41	($41.65)	0.17	(0.00)
6 months	$1,194.39	($90.78)	0.34	(0.01)	$1,297.09	($81.10)	0.34	(0.01)	$888.59	($99.61)	0.35	(0.01)
9 months	$1,684.83	($118.79)	0.50	(0.01)	$1,715.77	($117.94)	0.51	(0.01)	$1,320.51	($132.27)	0.53	(0.01)
12 months	$2,599.95	($220.19)	0.67	(0.01)	$2,360.60	($187.33)	0.67	(0.01)	$2,080.68	($225.26)	0.70	(0.01)
15 months	$3,406.31	($284.95)	0.84	(0.02)	$2,935.55	($232.62)	0.84	(0.02)	$2,769.26	($294.34)	0.88	(0.02)
18 months	$3,721.73	($278.60)	1.01	(0.02)	$3,269.52	($233.10)	1.01	(0.02)	$3,085.77	($290.69)	1.05	(0.02)

Mean (SE)
* Baseline Adjusted

Table 4.4 Cumulative Total Societal Costs and QALYs at each time period

	Walking				Walking + Behavioural				Self-directed			
	Total Costs($)		QALYs*		Total Costs($)		QALYs*		Total Costs($)		QALYs*	
3 months	$826.39	($58.97)	0.17	(0.00)	$919.65	($47.96)	0.17	(0.00)	$490.19	($55.54)	0.17	(0.00)
6 months	$1,251.52	($101.41)	0.34	(0.01)	$1,312.35	($81.85)	0.34	(0.01)	$1,093.46	($112.95)	0.35	(0.01)
9 months	$1,835.27	($137.41)	0.50	(0.01)	$1,738.63	($119.04)	0.51	(0.01)	$1,596.11	($150.55)	0.53	(0.01)
12 months	$2,583.58	($214.46)	0.67	(0.01)	$2,286.67	($175.86)	0.67	(0.01)	$2,241.76	($227.92)	0.70	(0.01)
15 months	$3,351.05	($286.00)	0.84	(0.02)	$2,798.67	($220.08)	0.84	(0.02)	$2,927.32	($288.70)	0.88	(0.02)
18 months	$3,922.44	($301.51)	1.01	(0.02)	$4,017.47	($236.50)	1.01	(0.02)	$3,471.08	($300.80)	1.05	(0.02)

Mean (SE)

* Baseline Adjusted

4.4.2 Adjusted Analysis

4.4.2.1 Purpose

An adjusted analysis was conducted to control for covariates which were believed to have a potential influence on cost and QOL outcomes. With a drop out rate of approximately 50% over the course of the study, an analysis adjusting for missing data was necessary. The selected covariates included: age (years), the duration of OA (years), gender, level of education (college/ university), obesity (BMI of 30kg/m^2 or greater), and level of intensity [total metabolic equivalent of task (MET) score]. Baseline costs and utility values were included in each respective analysis. The adjusted analysis allowed for the comparison of results using different methods for handing missing data and using simultaneous versus hierarchical regression models (Section 3.4).

4.4.2.2 Multiple Linear regression analysis using "stepwise" method

The stepwise procedure consisted of entering the covariate with smallest probability ($f \leq 0.05$) in the model while removing another covariate with a sufficiently large value ($f \geq 0.2$) at each stage (Section 3.4.3.2). After running the stepwise regression, SPSS was unable to produce an accurate final model as the analysis required coefficients from all 5 imputation sets to reach statistical significance. In this case, the stepwise procedure for pooled data was impossible as predictor sets in the final models differed according to various imputations.

4.4.2.3 Analyses including all covariates

All covariates which were believed to be clinically meaningful were simultaneously entered in the model. The independent coefficients illustrated how much the dependent cost/QALY variables were expected to increase or decrease if it increased by one unit, assuming all independent coefficients were held constant. Dummy variables for the W and WB groups provided a cost/QALY estimate, revealing the influence of the independent covariates when compared to the self-directed group (C).

Standardized coefficients (beta) were provided for the QALY regression analyses as the last value carried forward technique was used to replace missing variables in the QALYs dataset. Unstandardized coefficients (B) were provided for the health care and societal costs regression analyses as multiple imputation was used to replace missing values.

4.4.2.3.1 QALYs

At 18-months, the coefficients for W ($p=0.23$) and WB ($p=0.11$) suggested lower QALY scores than the self-directed group (C). QALY scores for W were 0.02 lower than the self-directed group (C) which compared to a difference of 0.04 in the unadjusted analysis. QALY scores for WB were 0.02 lower than the self-directed group (C) which compared to a difference of 0.04 in the unadjusted analysis (Tables 4.8 & 4.9). Two covariates were shown to be significant at the pre-specified level. For every year a patient had arthritis, his/her QALY score decreased by 0.085 ($p=0.085$) (Table 4.6). As expected there was a statistically significant ($p<0.001$) positive correlation between baseline utility values and QALY scores. Results at 12 and 15 months also suggest lower QALY scores for the W and WB groups (Appendices 4.5 & 4.6).

Table 4.5 Multiple Regression Analysis- Mean QALY score at 18 months

Covariate	QALY	SE	p
(Constant)	.439	.064	.000
W	-.018	.015	.228
WB	-.024	.015	.112
Obese	-.010	.012	.412
College	.012	.014	.382
Participant's Gender	.006	.013	.639
Participant's Age	-.001	.001	.243
How many years have you had arthritis?	-.001	.001	.085
TotalbaselineMETS	0.00	.000	.787
BaselineUtility	.950	.067	.000

Dependent Variable: Mean QALY at 18 months
Obese: $\geq$ 30kg/m^2;College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values

4.4.2.3.2 Health Care Costs

At 18-months, both the W (p=0.06) and WB groups (p=0.44) suggested increased health care costs when compared to the self-directed group. Mean health care costs for W were $750.15 higher than the self-directed group (C) which compared to a difference of $635.96 in the unadjusted analysis. Mean health care costs for WB were $304.28 higher than the self-directed group (C) which compared to a difference of $183.75 in the unadjusted analysis (Table 4.8). Two covariates were shown to be significant at the pre-specified level. Total health care costs decreased by $25.24 ($\pm$18.04) as age increased by one year (p=0.16). As expected, there were positive relationships between patient baseline costs and total health care costs (p<0.001) (Table 4.6). Higher health care costs were observed for both the W and WB groups at 12 (p=0.05 &

p=0.23 respectively) and 15 months (p=0.08 & p=0.49 respectively) when compared to the self-directed group (C) (Appendices 4.7& 4.8).

Table 4.6 Multiple Regression Analysis- Total Health Care Costs at 18 Months

Covariate	Cost ($)	SE	p
(Constant)	4321.243	1238.343	.000
W	750.151	401.123	.064
WB	304.282	395.463	.442
College	-8.905	352.447	.980
Obese	46.879	311.470	.880
How many years have you had arthritis?	-3.508	21.638	.871
Participant's Gender	253.309	332.332	.446
Participant's Age	-25.235	18.045	.162
PatientBaselineCosts	.853	.303	.005
TotalbaselineMETS	-2.479	2.779	.373

Dependent Variable: Mean Patient Cost at 18 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health care costs

4.4.2.3.3 Societal Costs

At 18-months, both the W (p=0.12) and WB groups (p=0.81) suggested increased health care costs when compared to the self-directed group (C). Mean societal costs for W were $635.60 higher than the self-directed group (C) which compared to a difference of $451.36 in the unadjusted analysis. Mean societal costs for WB were $99.17 higher than the self-directed group (C) which compared to WB having $150.84 lower costs compared to the self-directed group (C) in the unadjusted analysis (Table 4.9). Three covariates were shown to be significant at the pre-specified level. Total societal costs decreased by $28.36 ($\pm$12.47) at 12 months (p=0.02), $32.01 ($\pm$16.52) at 15 months (p=0.05), and $35.36 ($\pm$18.68) at 18 months (p=0.06), as age increased by

one year. As baseline intensity level scores increased by one, societal costs decreased by $3.76 (±2.02) at 12-months (p=0.64), $5.00 (±2.59) at 15 months (p=0.05), and 4.63 (±2.83) at 18 months (p=0.10). Once again, a positive relationships between societal baseline costs and total societal costs was observed (p<0.001) (Table 4.7). At 12 and 15 months, similar results revealed higher total societal costs for W and WB, with only the W group having statistically significant results (p=0.10 & p=0.15 respectively (Appendices 4.9 & 4.10).

Table 4.7 Multiple Regression Analysis- Total Societal Costs at 18 Months

Covariate	Cost ($)	SE	p
(Constant)	5135.545	1284.945	.000
W	635.596	406.445	.120
WB	99.169	401.005	.805
College	-2.009	361.180	.996
Obese	163.565	316.418	.605
How many years have you had arthritis?	5.592	21.983	.799
Participant's Gender	264.561	339.159	.435
Participant's Age	-35.362	18.680	.059
SocietalBaselineCosts	.978	.242	.000
TotalbaselineMETS	-4.627	2.832	.103

Dependent Variable: Mean Patient Cost at 18 months ($CAN)
Obese: ≥ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal costs

4.3.2.3.4 Cost Effectiveness

From the societal and the health care system perspective, the self directed program dominated the walking and walking plus behavioural programs in that it is less costly and patients had more QALYs (Tables 4.8 and 4.9). This was consistent in both the unadjusted and adjusted analyses.

Table 4.8 Adjusted and Unadjusted Health Care Costs and QALYs at 18 Months

	Walking vs. Self-directed		Walking + Behavioural vs. Self-directed	
	Incremental Cost	Incremental QALY	Incremental Cost	Incremental QALY
Adjusted	$750.15	-0.02	$304.28	-0.02
Unadjusted	$635.96	-0.04	$183.75	-0.04

Table 4.9 Adjusted and Unadjusted Societal Costs and QALYs at 18 Months

	Walking vs. Self-directed		Walking + Behavioural vs. Self-directed	
	Incremental Cost	Incremental QALY	Incremental Cost	Incremental QALY
Adjusted	$635.60	-0.02	$99.17	-0.02
Unadjusted	$451.36	-0.04	$-150.84	-0.04

4.5 Alternate Estimates of Cost Effectiveness

4.5.1 Purpose

The purpose of performing alternate estimates of cost effectiveness is to highlight differences between results when not allowing for missing and censored data. Separate analyses were performed for complete data only, imputed missing values with baseline data, and imputed missing values using multiple imputation.

4.5.1 Complete Case Analysis

In this analysis, total mean costs and QALYS were calculated at 18-months using data only from those patients who neither withdrew from the study nor had missing data (i.e. the patient had complete data) (Appendix 4.2). At 18-months, the complete case analysis revealed lower QALY

scores for the W and WB group than the self-directed group (C). QALY scores for W were 0.05 lower than the self-directed group (C). QALY scores for WB were 0.07 lower than the self-directed group (C)

Both the W and WB groups suggested increased health care costs when compared to the self-directed group (C). Mean health care costs for W were $1,209.54 higher than the self-directed group (C). Mean health care costs for WB were $424.98 higher than the self-directed group (C).

The W group had higher societal costs than the self-directed group (C). Mean societal costs for W were $508.31 higher than the self-directed group (C). The WB group showed lower societal costs compared to the self-directed group (C). Mean societal costs for WB were $348.26 lower than the self-directed group (C) (Table 4.10).

4.5.2 Data Excluding Drop-outs

This analysis focused on including patients who did not drop out of the study. Thus, total mean costs and QALYS were calculated for participants who missed one or more evaluations, but did not drop out of the study (Appendix 4.3). At 18-months, the analysis excluding all drop-outs revealed lower QALY scores for the W and WB group than the self-directed group (C). QALY scores for W and WB were both 0.07 lower than the self-directed group (C) (Tables 4.10).

Both the W and WB groups suggested increased health care costs when compared to the self-directed group (C). Mean health care costs for W were $1,245.15 higher than the self-directed group (C). Mean health care costs for WB were $301.24 higher than the self-directed group (C) (Table 4.10).

The W group had higher societal costs than the self-directed group (C). Mean societal costs for W were $590.38 higher than the self-directed group (C). The WB group showed lower societal costs compared to the self-directed group (C). Mean societal costs for WB were $410.12 lower than the self-directed group (C) (Table 4.10).

4.5.3 Data Excluding Imputations (Complete evaluations only)

In this analysis data were analyzed only for evaluations for which there were complete data. Thus, total mean costs and QALYS were calculated for all original raw data including participants who missed one or more evaluations and study drop-outs (Appendix 4.4). At 18-months, the analysis excluding imputations revealed lower QALY scores for the W and WB group than the self-directed group (C). QALY scores for W and WB were both 0.04 lower than the self-directed group (C) (Table 4.10).

Both the W and WB groups suggested increased health care costs when compared to the self-directed group (C) . Mean health care costs for W were $677.38 higher than the self-directed group (C). Mean health care costs for WB were $167.77 higher than the self-directed group (C) (Table 4.10).

The W group had higher societal costs than the self-directed group (C). Mean societal costs for W were $254.87 higher than the self-directed group (C). The WB group showed lower societal costs compared to the self-directed group (C). Mean societal costs for WB were $365.25 lower than the self-directed group (C) (Table 4.10).

Table 4.10 Incremental costs and QALYs by Alternative Analytical methods

	Walking vs. Self-directed			Walking + Behavioural vs. Self-directed		
	Incremental health care cost	Incremental societal cost	Incremental QALY	Incremental health care cost	Incremental societal cost	Incremental QALY
Base analysis (adjusted)	$750.15	$635.60	-0.02	$304.28	$99.17	-0.02
Unadjusted	$635.96	$451.36	-0.04	$183.75	$-150.84	-0.04
Complete case analysis	$1,209.54	$508.31	-0.05	$424.98	$-348.26	-0.07
Excluding drop outs	$1,245.15	$590.38	-0.07	$301.24	$-410.12	-0.07
Complete evaluations only	$677.38	$254.87	-0.04	$167.77	$-365.25	-0.04

4.5.4 Summary

The complete case analysis revealed differences in QALY scores among the W group (0.03) and WB group (0.05), health care costs among the W group ($750.69) and WB group ($120.70), and societal costs among the W group ($-127.29) and WB group ($-447.43). The analysis excluding drop-outs showed differences in QALY scores among the W group (0.05) and WB group (0.05), health care costs among the W group ($495.00) and WB group ($-3.04), and societal costs among the W group ($-45.22) and WB group ($-509.29).The analysis of data excluding imputations (complete evaluations only) revealed differences in QALY scores among the W group (0.03) and WB group (0.05), health care costs among the W group ($-72.77) and WB group ($-136.51), and societal costs among the W group ($-380.73) and WB group ($-464.42).

Although there is a difference in magnitude of these estimates, they provide the same interpretation and conclusion.

4.6 Incremental Net Benefit Analysis

4.6.1 Purpose

The purpose of the INB analysis was to investigate the uncertainty around the incremental cost-effectiveness of the W and WB interventions while controlling for covariates. The INB analysis allowed for the generation of CEACs, the exploration of EVPI, and investigation of heterogeneity. The INB analysis consisted of calculating an INB for each intervention, considering both societal and health care costs. INBs were calculated by multiplying QALY scores with a WTP threshold (λ) ($50, 000.00 per QALY), and subtracting the incremental costs (Section 3.4.4):

$$\mathbf{INB = \Delta_{QALY} \times \lambda - \Delta_{Cost}}$$

INB estimates were obtained from the regression analyses using the simultaneous method which included the following covariates: age (years), the duration of OA (years), gender, level of education (college/ university), obesity (BMI of 30kg/m^2 or greater), and level of intensity [total metabolic equivalent of task (MET) score], and baseline utility values/costs

4.6.2 Incremental Net Benefit

Figure 4.2 depicts the estimated incremental net benefit for W and WB compared to the self-directed group (C) for different values for a QALY for an 18-month time horizon and the health care system perspective. Figure 4.3 depicts the estimated incremental net benefit for W and WB compared to the self-directed group (C) for different values for a QALY for an 18 month time

horizon and the societal perspective. Appendices 4.11 to 4.14 provide the same figures for a 12 and 15 month time horizon.

With a WTP threshold (λ) of $50,000.00 per QALY, regression analysis results (Appendix 4.15) revealed the INB based on the health care payer perspective for the W group was -$1,515.13 (p=0.10) compared to the self directed group which highlights the lack of cost effectiveness of the W intervention. Similarly for WB, the INB was -$1,640.94 (p=0.08) compared to the self directed group.

Based on the societal perspective, with a WTP threshold (λ) of $50,000.00 per QALY, regression analysis results (Appendix 4.16) revealed that the INB for the W group was -$1,378.22 (p= 0.14) compared to the self directed group, revealing that it was not a cost effective intervention. The WB was also not cost-effective with an INB of -$1,402.76 (p=0.14) compared to the self-directed group.

No significant differences in INB results were observed from either the health care payer perspective at 12 (Appendix 4.17) and 15 months (Appendix 4.18), nor from the societal perspective at 12 (Appendix 4.19) and 15 months (Appendix 4.20).

Figure 4.2 Incremental Net Benefit of Walking Programs versus Self Directed Program - Health Care Costs at 18 months

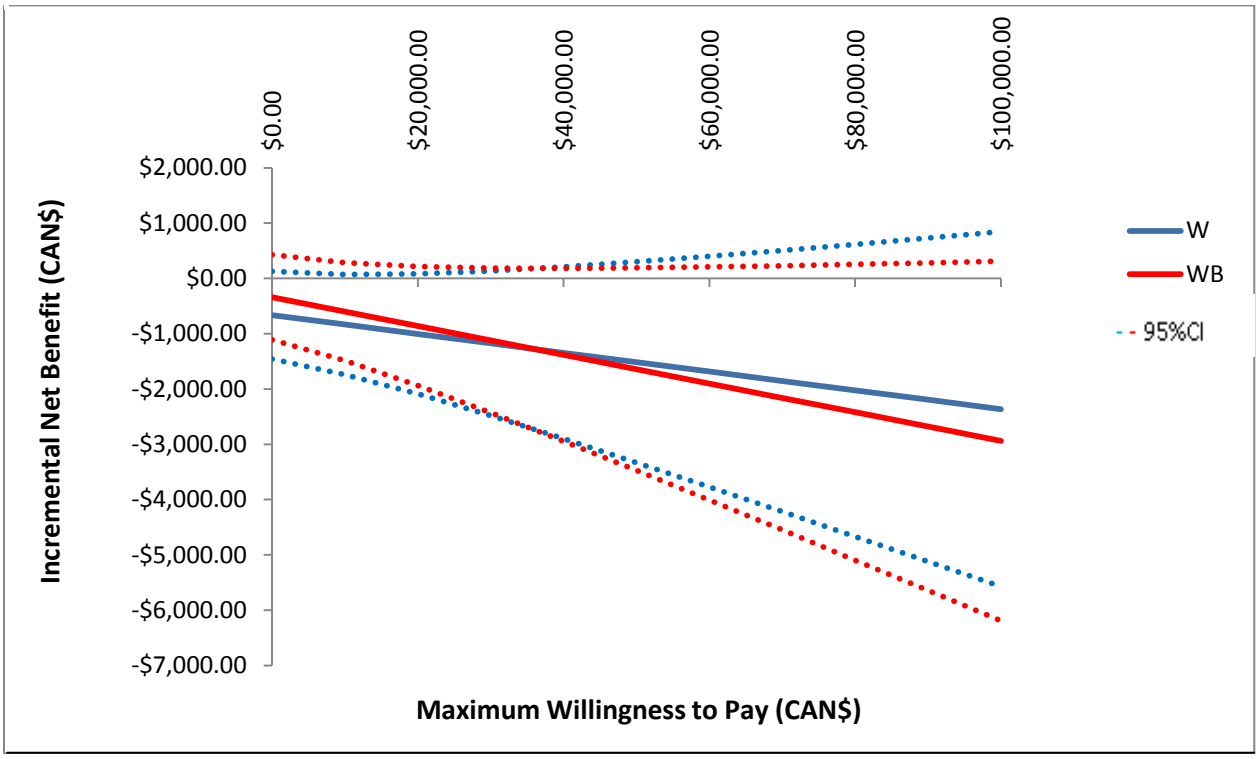
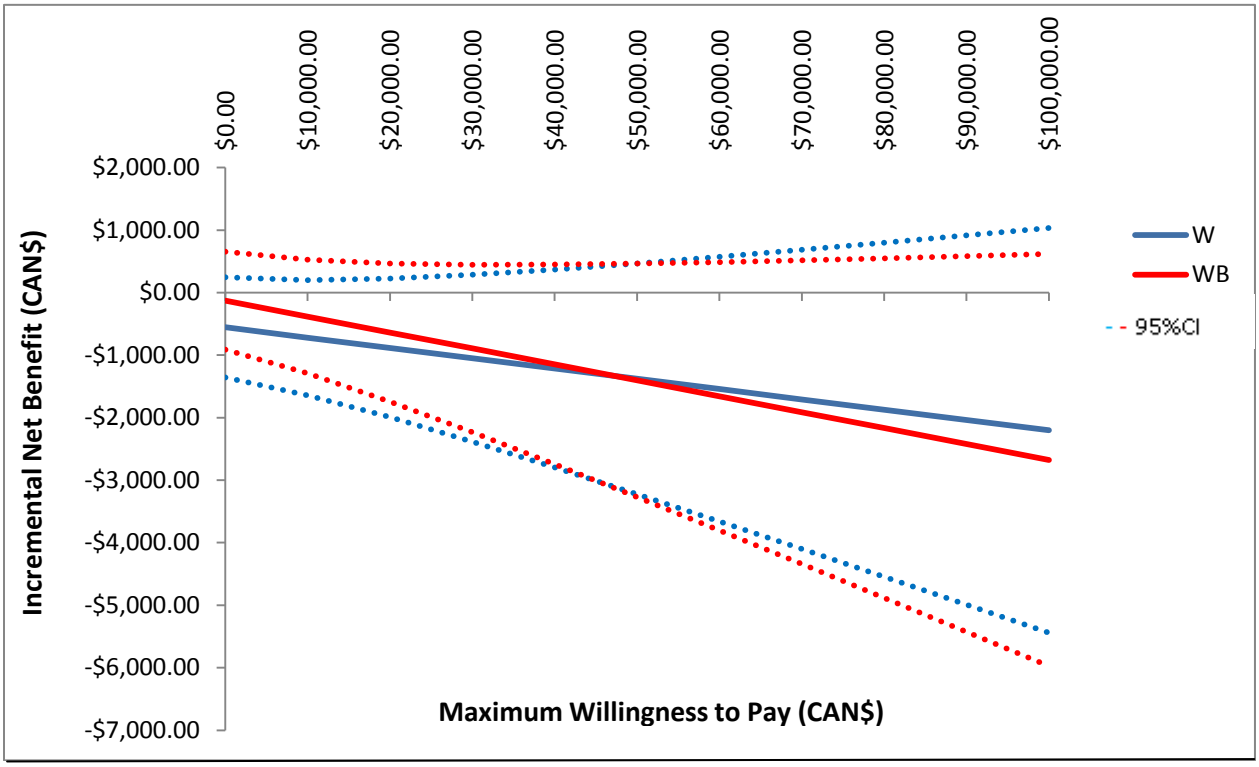


Figure 4.3 Incremental Net Be Net Benefit of Walking Programs versus Self Directed Program - Societal Costs at 18 months



4.6.3 Cost-Effectiveness Acceptability Curves

Figure 4.4 depicts the probability that each intervention as optimal using the health care payer perspective at 18 months with a WTP threshold of $50,000 per QALY was 91.36 %, 4.82%, and 3.82% respectively for the self-directed, W and WB interventions Figure 4.5 depicts the probability that each intervention as optimal using the societal perspective at 18 months with a WTP threshold of $50,000 per QALY was 86.86 %, 6.86%, and 6.28% respectively for the self-directed, W and WB interventions.

Only marginal differences were seen in the shapes of the CEACs for analysis from the health care payer's perspective at 12 (Appendix 4.21) and 15 months (Appendix 4.22), and from the societal perspective at 12 (Appendix 4.23) and15 months (Appendix 4.24).

Figure 4.4 CEAC Health Care Costs at 18 Months

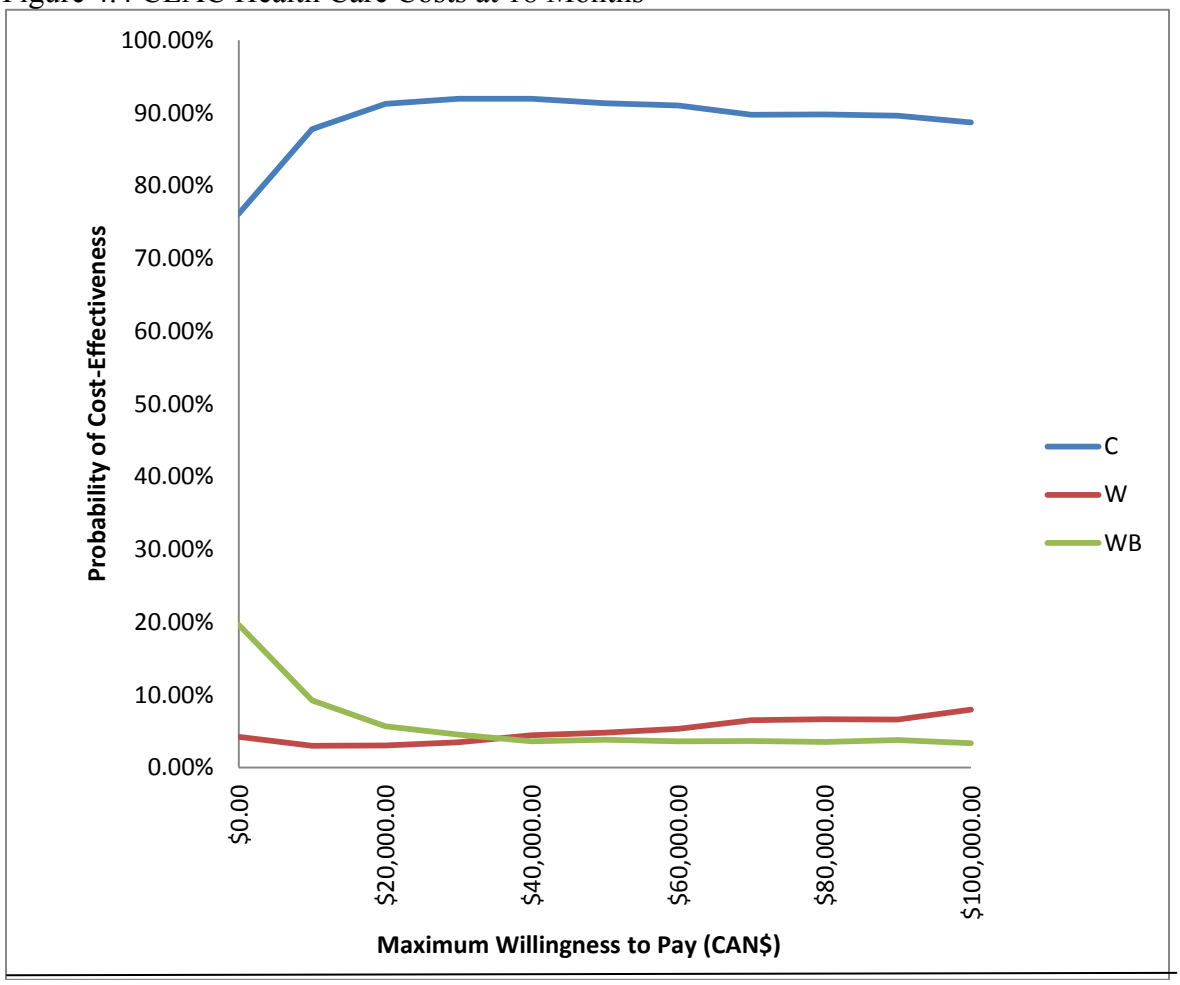
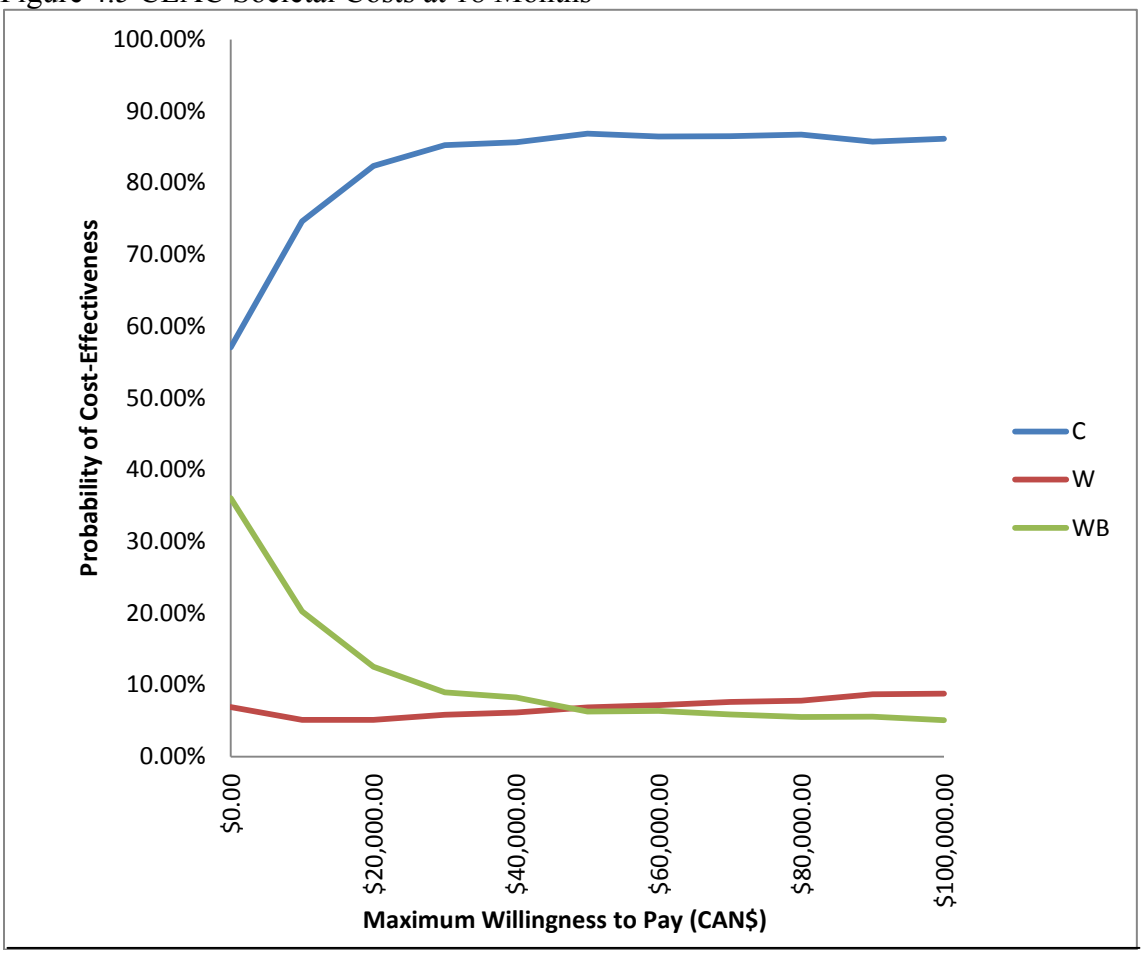


Figure 4.5 CEAC Societal Costs at 18 Months



4.6.4 Expected Value of Perfect Information

Figure 4.6 depicts the EVPI, the maximum amount a decision maker is willing to spend to reduce the uncertainty and acquire additional evidence on for future decisions, of supervised aerobic walking programs using health care cost data at 12, 15, and 18 months. Figure 4.7 illustrates the EVPI for supervised aerobic walking programs using societal cost data at 12, 15, and 18 months.

The expected value of perfect information analysis revealed that with a maximum WTP threshold of $50,000 per QALY, the mean value of further research per person was $13.38 at 12 months, $30.60 at 15 months, and $35.64 at 18 months based on health care costs. Using mean

societal costs, the mean value of further research was $24.31 at 12 months, $47.03 at 15 months, and $56.56 at 18 months respectively.

Figure 4.6 Expected Value of Perfect Information using Health Care Costs at 12, 15 and 18 months

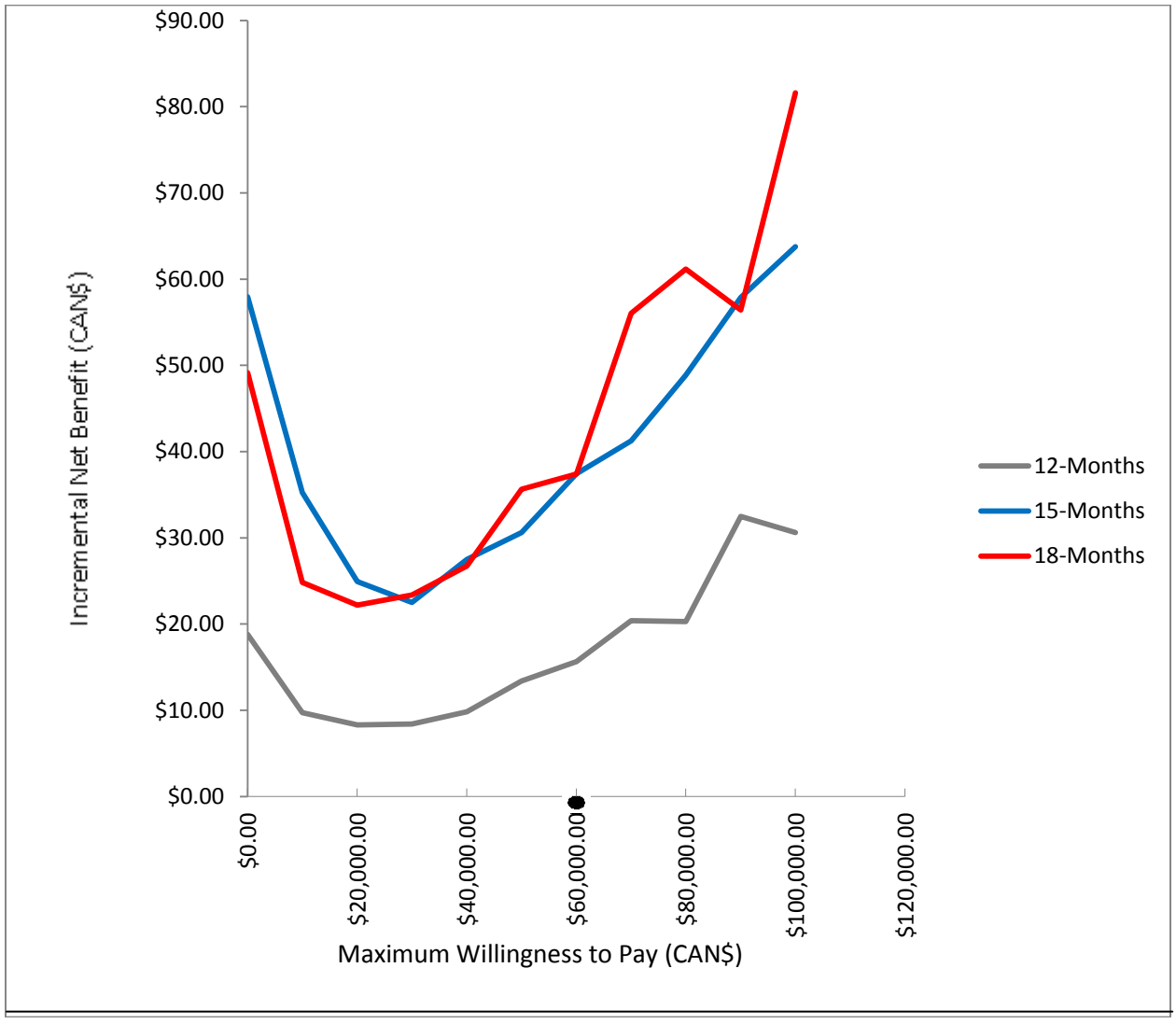
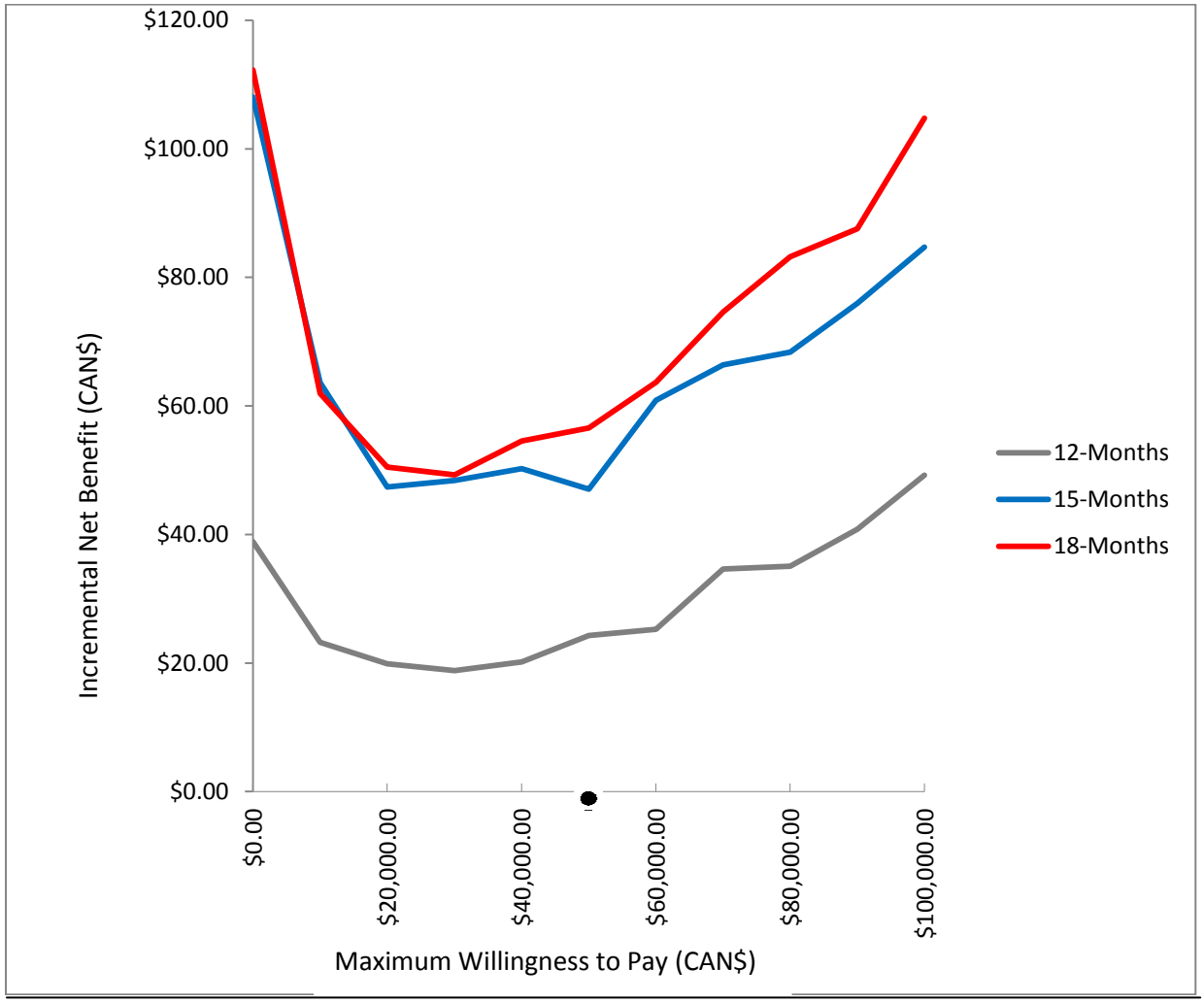


Figure 4.7 Expected Value of Perfect Information using Societal Costs at 12, 15 and 18 months



4.7 Sensitivity analysis results

Subgroup analyses were performed, comparing participants in the W and WB groups who were under the mean age of 63.4 years, females, had OA for less than 10.3 years (mean duration), obese ($\geq$30kg/m^2), and those who had a minimum college education. The sensitivity analysis was conducted from the perspective of the health care payer using of a multiple linear regression

analysis to measure the INB of each subgroup at 18-months. A WTP threshold of $50,000.00 was selected to determine if there was statistical significance among any of the covariates. Results revealed no significant differences among any of the specific subgroups (Table 4.11).

4.8 Conclusion

The unadjusted analysis, at 18 months, using multiple imputation to consider missing data from the high study drop out rate, revealed that the W group had the highest costs from both the health care and societal perspective. The self-directed group (C) demonstrated the lowest total costs from the perspective of the health care payer, while the WB group had the lowest costs from the societal perspective. The self-directed group (C) had higher QALY scores, both baseline adjusted and unadjusted, than the other two groups. Similar results were seen in all analyses at 12 and 15 months. Thus, analysis found that the self directed program dominates both the walking programs as it is less costly and patients gained more QALYs.

The adjusted analysis, performing a multiple linear regression analysis using the simultaneous method, revealed similar QALY and cost results compared to the unadjusted analysis. Slightly smaller incremental QALY scores and marginally larger incremental health care costs were seen when W and WB were compared to the self-directed group (C) at 18 months. The adjusted analysis revealed that the WB group did indeed have higher societal costs compared to the self-directed group (C). Thus, analysis reached the same conclusion that the self-directed program dominates both the walking programs as it is less costly and patients gained more QALYs.

Alternate estimates of cost-effectiveness produced similar conclusion to that of the unadjusted analysis. Larger incremental QALYs, societal and health care costs were seen for both W and WB when compared to the self-directed group (C) using only complete data and when excluding

drop-outs. Incremental QALY and costs results were most similar to the unadjusted analysis when imputations were excluded.

The INB analyses performed from the health care and societal perspective confirmed that both the W and WB interventions were not cost-effective in comparison to the self-directed intervention, again through being dominated by the self-directed program. The CEAC graphs highlighted that the self-directed intervention had a much higher probability of being the optimal intervention. The EVPI analysis concluded that there is not a great value for further information. The sensitivity analysis revealed no statistically significant subgroup differences among the study population.

Table 4.11.Linear Regression Analysis of Incremental Net Benefit using Health Care Costs with a WTP threshold of $50,000.00 at 18 months

Covariate	INB ($)	SE	p
(Constant)	2868.819	5918.678	.628
W	987.153	2299.173	.668
WB	-2640.039	2412.911	.274
How many years have you had arthritis?	19.214	65.897	.771
Obese	-617.408	1299.674	.635
College	41.289	1616.894	.980
TotalbaselineMETS	3.397	6.930	.624
PatientBaselineCosts	-1.099	.768	.153
BaselineUtility	50510.577	4267.246	.000
WAge	2058.067	1321.498	.119
WBAge	728.778	1392.554	.601
WGender	1818.992	1343.427	.176
WBGender	-273.295	1568.851	.862
WDuration	3017.804	2423.759	.213
WBDuration	4482.916	2414.524	.063
WObesity	-2093.191	1879.888	.266
WBObesity	1659.513	1842.540	.368
WCollege	177.176	2091.158	.932
WBCollege	1405.250	2160.092	.515

W= Walking Group; WB= Walking and Behavioural Group; WAge= Walking Group and under the age of 63.4 (mean age); WBAge= Walking and Behavioural Group and under the age of 63.4 (mean age); WGender= Females in the Walking Group; WBGender=Females in the Walking and Behavioural Group; WDuration= Walking Group and mean duration of OA <10.3 years (mean duration); WBDuration= Walking and Behavioural Group and mean duration of OA <10.3 years (mean duration); WObesity= Walking Group and obese ($\geq$ 30kg/m^2); WBObesity= Walking and Behavioural Group and obese ($\geq$ 30kg/m^2); College= Walking Group and education of some college or more; WBCollege= Walking and Behavioural Group and education of some college or more.

Chapter V

DISCUSSION

The following chapter is presented in two parts. The first part provides a discussion of the economic evaluation analysis results. Utility values, QALY scores, health care resource use, and INB results are discussed. Limitations of the economic evaluation are addressed. The second part of this chapter provides a comprehensive policy discussion regarding funding of aerobic walking programs in the management of knee OA. Evidence to support funding of physical activity programs is discussed highlighting the importance of physical activity for the prevention and management OA. Considerations for public health policy makers, organizational support for walking programs, and the current situation with respect to funding of exercise programs are described.

5.1. Economic Evaluation

5.1.1 Utility values and QALYs

Surprisingly, the supervised walking interventions (W and WB groups) had no impact on participants' utility. As time progressed, utility values decreased for the WB group while utility values of the self-directed group (C group) improved slightly when compared to baseline. Overall, the supervised walking interventions achieved similar lower QALY scores when compared to the self-directed group (C). Physical activity interventions, including walking programs, have improved QOL over a short-term period, when compared to "non-walking" control groups (55) (102) (53) (56) (155) (156) (157). Similar to the results of this study, supervised physical activity interventions do not always improve QOL over long-term durations (156) (56) (158). Reasoning as to why the self-directed group (C) demonstrated higher utility and

QOL scores may be due to the fact that this group may not have faced as many barriers as the other two groups. However, regression techniques to control for baseline health status were employed and did not affect the initial interpretation of the results.

Common barriers to engaging in walking faced by OA patients include time commitment (159), perceptions about illness and recovery, transportation difficulties, family commitments and inconvenient timing (160). The self-directed group (C) did not require access to transportation to attend an onsite walking program with specific hours of operation as they had the convenience of participating in walking activities at home or in a familiar environment. The self-directed intervention may also have been a more convenient means of physical activity for individuals who were not retired and were still working. Another interesting point was that the The self-directed group (C) exhibited the highest dropout rate. It is uncertain if only healthy participants with an improved QOL decided to continue walking and adhere to the intervention. Analysis did adopt the most appropriate methods for handling missing and censored data, which may in some way alleviate these concerns.

5.1.2 Health Care Resource Use

When comparing the health resource use among the three groups, it appears that the self-directed group (C) incurred the lowest total health care costs compared to the other two comparative groups. The self-directed group (C) demonstrated the lowest mean costs for physician specialists, diagnostic tests, laboratory tests, and medication intake. With the least amount of health care resource use, it appears that the self-directed group (C) was either overall a healthier group, or were more independent having a greater perceived ability to manage their own health. At 18-

months, the self-directed group (C) demonstrated the highest "confidence about doing things" score (p=0.048) on the Stanford Chronic Disease Questionnaire. This result suggests that the self-directed group (C), being unsupervised, was more likely to have greater self-confidence and self-efficacy skills compared to the other two supervised walking groups. Similarly to the self-directed group (C) of this study, qualitative studies have shown that older individuals with chronic conditions and dependent mindsets towards managing their conditions utilized a greater amount of health resources with more frequent readmissions to acute care hospitals (161) (162).

5.1.3 Incremental Net Benefit

Given the low probability that either walking interventions would be cost-effective and that the results of the EVPI analysis found little additional value for further information, it is unlikely that additional research would be an efficient use of scarce resources.

5.1.3 Limitations

A limitation of the RCT was the nature of the self-directed control group as participants in this group were very active having received an educational pamphlet on OA which recommended walking regularly (3 to 5 times a week). The initial rationale of providing participants in the self-directed group (C) with pedometers and logbooks was for measurement purposes, although it appears that these tools may have actually motivated participants. As a result, participants' self-reported logbook reports depicted that this group walked regularly and most likely benefitted from the walking intervention just as much as the other two supervised walking groups. A high attrition rate in all three groups may create concern regarding the validity of long term results at 12 and 18 months. There is a possibility of selection bias as the study population only included

individuals with mild to moderate OA who must have had a confirmed X-ray report. The study also included a mix of retired and employed participants. A five-month bus-strike and extreme winter weather conditions also had a greater negative impact on study compliance among those in the W and WB groups.

A major limitation of this economic evaluation was the health resource utilization questionnaire. The questionnaire provided to participants was not a generic osteoarthritis specific as some questions were broad and included various health resources. Since the questionnaire was refined to be more OA specific after being completed by the participants, responses were assumed to be related to their arthritic conditions. Another limitation of the economic analysis was the estimation of drug costs. Since the exact dosage of the drugs used by participants was unknown, dosages were estimated using product monographs of each identified medication.

5.1.4 Conclusion

Results of the economic evaluation revealed that unsupervised self-directed program compared to the supervised walking and the combined walking and behavioural interventions appeared to be the most cost-effective approach from both a societal and health care payer's perspective. The cost of the self-directed control intervention much smaller than the costs of the two walking intervention. Higher QALY scores, greatest improvements in utility and lowest health care costs were observed for participants in the self-directed group (C). Furthermore, the expected value of perfect information analysis revealed that further research comparing the cost effectiveness of the three interventions is unlikely to be worthwhile. Although the two supervised walking programs were not cost-effective, all three interventions demonstrated equivalent results in terms of clinical outcomes such as pain, functional status, mobility and endurance improved throughout

the 18-month duration. Therefore, walking, either supervised in a community setting, or unsupervised in a home setting may be a favourable non-pharmacological option for the treatment and management of OA of the knee. It may be inferred from this analysis that it would be cost effective for a health care ministry to cover the costs of a self-directed walking program for individuals with OA of the knee; including pedometers, logbooks and educational pamphlets on walking and OA compared to covering the costs of arthritis medications and surgeries.

5.2 Evidence to support funding of physical activity programs in the management of knee OA

5.2.1. Importance of physical activity to prevent and manage OA

OA patients have become more inactive over time (163). This lack of physical activity has resulted in reduced mobility, loss of independence, and reduced QOL (164). Physical activity enhances health and may prevent disability and functional loss (56). According to Ottawa Panel guidelines, walking programs can increase muscle strength, aerobic capacity and reduce functional limitation OA (48) (46) (47). In order for exercise programs to be effective in preventing and reducing the progression of OA, they must consist of physical activity that is light and moderate where the frequency and intensity is not at a level where it will aggravate the joints of individuals (56).

5.2.2 Systematic review of aerobic walking programs for OA

The Ottawa Panel performed a systematic review and developed evidence-based clinical practice guidelines on aerobic walking programs for the management of OA of the knee and hip (165). This systematic review provides new evidence regarding the benefits of structured aerobic walking programs for knee OA patients. The author's reviewed 9 randomized controlled trials

(RCTs) (166) (53) (55) (57) (56) (167) (168) (58) (156) and one controlled clinical trial (CCT) (59), all which presented a supervised aerobic walking program intervention for the experimental groups and were compared to a non-walking control group. The participants in the ten studies were aged 40 years or older and presented radiographic evidence of primary knee OA. The authors assessed the methodological quality of each study using the 5-point Jadad scale (169) and The Cochrane Collaboration methods (www.cochrane.org) were used to perform statistical analysis. Two RCTs (55) (168) compared a walking program combined with strength training to an educational session control group. Three RCTs (166) (53) (58) compared a walking program combined with health education and behavioural components to an educational session control group. Two RCTs compared walking programs which included a multi-component exercise intervention to an educational session and telephone support control group (167) and to a control group which performed active range of motion, isometric strengthening, and relaxation exercises (156). The final two RCTs compared a walking program combined with multi-component exercises and health education to an educational session control group (55) (56). The CCT compared a walking program to individuals who were asked to continue their normal daily activities (59).

The Ottawa Panel concluded that seven (166) (53) (57) (56) (168) (58) (156) of the ten previously mentioned studies obtained high methodological quality according to the Jadad scale. Evidence suggested that aerobic walking programs, either facility, hospital, or home-based offered solely or in combination with other therapies if an effective intervention for both short and long-term management of mild to moderate OA of the knee and hip. Results from this systematic review revealed that walking programs can improve pain and stiffness, mobility, strength, endurance, functional status, and QOL.

5.2.3. Considerations for public health policy makers

Clinical practice guidelines, such as those by the Ottawa Panel on aerobic walking programs for the management of OA of the knee and hip provides important information for patients, physiotherapists, physicians, educators, health administrators and government policy makers. OA conditions differ among patients, creating a challenge for health professionals to treat and prescribe effective therapeutics. As the effects of OA are irreversible, it is important to provide OA patients with low-cost treatment before their conditions worsen and before more expensive and invasive interventions are required. Clinical practice guidelines by the Osteoarthritis Research Society International (OARSI) (117) suggests the use of pharmacological modalities such as acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular injections, and opioids to improve pain relief and reduce inflammation. For more severe OA cases, OARSI recommends surgical modalities including total knee or hip replacements, osteotomies to shorten, lengthen or change bone alignment, knee fusion, and knee aspiration using joint lavage to wash blood, fluid or debris from the joint space. Structured aerobic walking programs provide a more economical alternative as an effective management and preventative strategy which can save both patient and healthcare costs.

Updated OARSI recommendations (117) based on the best available evidence of 64 systematic reviews have summarized the strengths and weaknesses of various OA treatments. Electromagnetic therapy has shown small improvements in physical function and no significant reduction in pain (170). Acupuncture has shown to be efficacious for pain relief and physical function (117), however these improvements appeared to diminish over time (171). Although opiods have shown to moderately improve pain and physical function, these substances have been associated with multiple side effects such as nausea, constipation, dizziness, somnolence

and vomiting (117). Acetaminophen has shown to have no significant effect for pain reduction (172), stiffness, or physical function, and may have upper gastrointestinal side effects (173). NSAIDs have shown to be moderately more successful for reducing pain than acetaminophen (174) but have also been associated with gastrointestinal bleeding among a high risk population (175). More invasive surgical procedures such as arthroscopic debridement concluded that there were no benefits among knee OA patients (176). Tibial osteotomy is efficacious for reducing pain and improving function (177), but has a failure rate of 25% over 10 years (178).

Recent systematic reviews (179) (180) (181) (182) (46) (48) have shown that both strengthening and aerobic exercise reduce pain and improve functional ability among knee OA patients. Exercise programs consisting of functional and aerobic activities were more cost-effective when compared to usual primary care (77) and outpatient physiotherapy (6). A study in the U.K. concluded that an exercise program consisting of strengthening and aerobic exercise is a cost-effective approach if payers are willing to spend £8000 per patient for a 50% improvement in knee pain (86). The supplementation of an educational component to a home-based exercise program improved cost-effectiveness when compared to the home-based exercise program alone (79). Exercise programs can provide several physiological benefits for arthritis patients such as reducing the risk of coronary artery disease, serum lipid abnormalities, hypertension, diabetes, osteoporosis, obesity, and colon cancer (183) and enhances stamina by reducing fatigue and improving sleep (184). In addition, exercise programs provide several psychological benefits such as decreased anxiety, improved mood and state of relaxation (183).

The Arthritis Alliance of Canada reported that over the following 30 years, adequate pain management strategies would result in cumulative savings of $488 billion, while weight reduction strategies among obese (BMI $\geq$ 30) would could prevent over 200, 000 new OA cases and savings of $212 billion (185). The Ottawa Panel developed clinical practice guidelines concluding that physical activity, such as walking programs, are beneficial for pain relief, functional status, and weight loss among obese or overweight adults with OA (47). Given this evidence, it is apparent that the implementation of walking programs will provide vast health care and wage-based productivity cost savings over long-term.

5.2.4 Organizational support for walking programs

Specific health maintenance organizations such as Arthritis Consumer Experts (www.jointhealth.org) and The Arthritis Society (TAS) (www.arthritis.ca) offer several self-management programs that promote the maintenance of regular, moderate intensity physical activity for the treatment and management of osteoarthritis. Some of these programs which include arthritis education, self-management and coping skills, and exercise programs are funded by the Ontario Ministry of Health and Long-term Care (186). Provincial organizations, such as the British Columbia Recreation and Parks Association offer physical activity and walking programs and also provide grants to set up activity programs such as walking clubs. The Heart and Stroke Foundation of British Columbia developed the "Hearts in Motion Walking Club" with over 40 walking clubs in various communities in British Columbia being established (187). A membership fee of $10.00 provides participants with educational material and bi-annual newsletter subscription. At the municipal level, several community-based walking clubs either indoors, such as mall walking, or outdoor hiking programs have been growing in popularity in

Canada (188). Walking programs can be easily implemented with existing walking clubs that are administered by municipal public health programs. These programs typically require an inexpensive annual membership fee. Walking programs from around the world, such as "WALK 2000" (189), a walking program in Birmingham, England, and "Just Walk It" (190), with 4500 participants in 75 cities and towns across Queensland, Australia, promote safe walking to individuals to increase their level of fitness and promote better health. The programs are free of charge as they are both government funded. These are excellent examples of collaboration between government and best-practices researchers to create physical activity programs which promote the vast health benefits of walking.

5.3 Current situation with respect to funding of exercise programs

5.3.1 Funding of exercise programs in Canada

Revenue to support exercise programs in Canada are dependent on local funding opportunities and community investment. Sources of revenue include program fees and donations, community contributions, corporate sponsorships, and special event fundraising (191). In some cases, start-up funding is available through government grants such as the *Get Fit for Active Living* program (192) funded by the Public Health Agency of Canada (PHAC), or by non-profit organizations such as the Victorian Order of Nurses' *Senior's Maintaining Actives Roles Together (SMART)* program (193) funded by the Ontario Trillium Foundation. Exercise program expenses generally include staffing, promotion and marketing, materials and supplies, equipment, and space (191).

Though federal government agencies, such as PHAC, provide physical activity guidelines and continue to promote physical activity (194), provincial insurance plans still do not cover exercise program fees. The Canada Health Act provides a clear distinction between "insured health

services" and "extended health services" (195). Provincial insurance plans cover only health services which are deemed to be "medically necessary". Given that exercise programs are not subject to the criteria in the Act, membership fees and expenses are considered to be extended health care services and are charged at full private rates. Interestingly enough, other extended health care services, which are also not subject to the Act, such as optometric services, dental care, assistive devices and prescription drugs, may be covered by provincial plans, and are typically covered by private insurance plans. The Government of Canada recently passed a tax credit program for young individuals under the age of 17 years who are registered in an approved organized sport or physical activity program. Similar initiatives to promote physical activity among older Canadians are therefore needed to facilitate and reduce the economical barriers of engaging in exercise programs such as a walking program.

5.3.2 Evidence to support the cost-effective of exercise for other chronic conditions

Exercise programs have shown to be cost-effective for other chronic conditions such as rotator cuff disease, low back pain, coronary artery disease, heart failure, and hypertension. A systematic review identified the cost-effectiveness of exercise-based interventions in the treatment of various diseases (114). Among the 151 articles which were closely reviewed, exercise interventions were deemed to be cost-effective in 60 percent of cardiology cases and 54 percent in musculoskeletal disorders.

A six-month supervised exercise program for the treatment of rotator cuff disease, consisting of rotation, flexion-extension, and abduction-adduction repetitive movements for an hour a day, twice a week, was more cost-effective than soft laser treatment (196).

A supervised exercise program in the treatment of low back pain, consisting of eight one-hour group sessions including low impact aerobic exercises, strengthening exercises and stretching, was more clinically effective and cost-effective than usual care after 6 months (197).

A two-year cardiac rehabilitation and prevention program, consisting mostly of aerobic exercise demonstrated a reduced health care cost per patient and $640 saved per QALY gained when compared to conventional care (198).

Exercise training compared to percutaneous transluminal angioplasty (PTA) among patients with peripheral arterial disease revealed a cost savings of $61.00 per meter walked for the exercise group after 6 months concluding that exercise can effectively treat claudication as well as pharmacological and surgical interventions with fewer costs (199).

A 14-month long exercise training program consisting of stretching and 40 minutes of cycling, three times a week, revealed a cost-effectiveness ratio of $1,773 per life-year saved among heart failure patients (200). Exercise consisting of stationary cycling during hemodialysis treatments produced an average annual cost saving of $885 per patient-year in the exercise group when compared to usual care (201).

5.3.3 Implications of an aging population

With an aging Canadian population, the incidence of chronic diseases has increased to 80% among seniors living at home (202). In addition, injuries among this age group a serious concern with close to half of all injuries occurring at home (203). As a result, seniors tend to use more health services and are more likely to be hospitalized, for longer durations, when compared to other age groups in Canada (202). Exercise programs and physical activity can reduce the rate of

bone loss, improve strength and flexibility, balance and coordination, and can help reduce the risk of falls and injuries (194) (204). In addition, exercise programs can improve independence while prolong good health (205).

5.4 Overall conclusion

The results of the systematic review revealed that there is a limited amount of high-quality economic evaluation studies examining the cost-effectiveness of exercise interventions for the treatment of OA. Results of the cost-utility analysis suggested that a self-directed walking program may be a more cost-effective approach compared to a supervised walking program either supplemented with an educational intervention or not. All three walking interventions appeared to improve OA symptoms, concurring with similar studies assessing aerobic walking in the treatment of knee OA (48). There is a sufficient amount of evidence to support the consideration of funding community-based aerobic walking programs, whether supervised or not, to promote health and improve the disabling symptoms of OA. The presented evidence suggests that funding form the provincial government for aerobic walking programs can improve OA symptoms and potentially reduce the economic burden of more costly health care resources. Aerobic walking programs are worthy of reimbursement, specifically among high- risk OA populations.

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Appendices

Appendix 2.1 Search strategies for Identifying Studies Concerned with Cost-Effectiveness of Exercise Interventions in the treatment of mild to moderate osteoarthritis of the knee

Medline (until July 2011)

1 Osteoarthritis/
2 osteoarthritis, knee/
3 arthrit* knee.ti,ab.
4 osteoarthritis.ti,ab.
5 1 or 2 or 3 or 4
6 walking/
7 exercise therapy/
8 walking program*.ti,ab.
9 aerobic.ti,ab.
10 6 or 7 or 8 or 9
11 cost benefit analysis/
12 exp health care costs/
13 cost effectiveness*.ti,ab.
14 cost benefit analys*.ti,ab.
15 health care cost*.ti,ab.
16 Quality-Adjusted Life Years/
17 quality of life/
18 economics.fs.
19 health care utilization.ti,ab.
20 quality of life.ti,ab.
21 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 22 5 and 10 and 21

Embase (until July 2011)

1 osteoarthritis/ or knee osteoarthritis/
2 osteoarthritis.ti,ab.
3 arthrit* knee.ti,ab.
4 1 or 2 or 3
5 exercise/ or aerobic exercise/
6 walking/
7 walking program*.ti,ab.
8 aerobic.ti,ab.
9 5 or 6 or 7 or 8
10 health care utilization/
11 exp "quality of life"/
12 "cost utility analysis"/
13 cost benefit analysis/
14 exp health care cost/
15 cost effectiveness analysis/
16 exp health economics/
17 cost/
18 cost effectiveness*.ti,ab.
19 cost benefit analys*.ti,ab.
20 health care cost*.ti,ab.
21 health care utilization.ti,ab.
22 quality of life.ti,ab.
23 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24 4 and 9 and 23

Cochrane Library (until July 2011)

#1 (cost*):ti,ab,kw

#2 (osteoarthritis):ti,ab,kw
#3 (arthriti* knee):ti,ab,kw
#4 (walking):ti,ab,kw
#5 (aerobic):ti,ab,kw
#6 (#1 AND (#2 OR #3) AND (#4 OR #5))

Appendix 2.2 Permission from Centre for Review and Dissemination

Dear Gino,

Your request to present NHS EED abstracts in the appendices of your thesis has been passed to me, as project lead. We are happy for you to use the abstracts, on the condition that they are appropriately referenced. I am glad that you found them useful and wish you every success with your thesis. If I can be of any further assistance please feel free to contact me directly.

Best wishes

Dawn

Dawn Craig
Research Fellow in Health Economics
Centre for Reviews and Dissemination
University of York

Appendix 2.3 Centre for Review and Dissemination (University of York) Summaries of Included Studies

Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain

Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Williamson E, Jones RH, Reeves BC, Dieppe PA, Patel A

CRD summary
The objective was to assess the cost-effectiveness of individual or group rehabilitation, compared with usual primary care, for the management of chronic knee pain. The authors concluded that rehabilitation, particularly group rehabilitation, was cost-effective. The methods were sound and the study was well reported. The authors' conclusions appear to be appropriate for the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to compare the cost-effectiveness of three strategies for the management of patients, aged 50 years or older, who had experienced mild, moderate, or severe knee pain, for over six months.

Interventions
The three interventions were: usual primary care; usual primary care combined with a rehabilitation programme delivered to individual participants; and usual primary care combined with the same rehabilitation programme delivered to groups of eight participants.

The rehabilitation programme consisted of 12 supervised sessions twice-a-week for six weeks. The first 10 to 15 minutes of each session was a discussion, run by the supervising physiotherapist, on a specific topic, with the provision of advice and coping methods. The next 30 to 45 minutes consisted of a programme of simple exercises that were intended to improve participants' functioning.

Location/setting
UK/primary care.

Methods
Analytical approach:
The economic analysis had a time horizon of six months and was based on a single clinical trial. The authors reported that a health and social care perspective and a societal perspective were adopted.
Effectiveness data:
The clinical data came from a pragmatic cluster randomised controlled trial. The sample consisted of 418 patients (294 women), with 140 in usual care, 146 in individual rehabilitation, and 132 in group rehabilitation. The three intervention groups were comparable at baseline in their clinical and socio-demographic characteristics, but they differed in their receipt of social security benefits at baseline. The follow-up was six months and further details were published in another paper (Hurley, et al. 2007, see 'Other Publications of Related Interest' below for bibliographic details). The primary endpoint was clinical improvement in self-reported functioning, measured by the physical function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-func) at six months after completion of the six-week rehabilitation.
Monetary benefit and utility valuations:
The utility values were derived from the trial participants, using the European Quality of life (EQ-5D) questionnaire. QALYs were calculated using utility weights from the UK general population.
Measure of benefit:
Improvement in functioning, based on a 15% increase in WOMAC-func from baseline, and quality-adjusted life-years

(QALYs) were the summary measures of benefit.

Cost data:

The economic analysis included: in-patient and out-patient services; community-based services; medications; hospital, laboratory, and screening tests; social security benefits; informal care (including personal care, home maintenance, housework and laundry, transport, preparing meals, shopping, and gardening); and productivity losses. Resource use was calculated retrospectively at baseline and at follow-up, using a subsample of 338 (81%) participants. The unit costs were based on national statistics. All costs were appropriately adjusted for inflation and reported for the price year 2003 to 2004. They were reported in UK pounds sterling (£) and US dollars ($) using a conversion rate based on the 2003 purchasing power parity, where £1 equalled $1.613.

Analysis of uncertainty:

Two sets of deterministic sensitivity analyses were performed. Uncertainty around the rehabilitation costs was investigated, using six different calculation methods and uncertainty around the total costs was investigated by varying the medication and informal care costs. All assumptions that were tested in the sensitivity analysis were reported. The uncertainty in the cost-effectiveness results was investigated using probabilistic analysis and cost-effectiveness acceptability curves were generated.

Results

At six months there were no statistically significant differences between the interventions in their QALYs gained. The difference in the proportion of patients with improvement in clinical functioning was statistically significant, with 121 of 226 in the rehabilitation groups and 47 of 113 in the usual care group (χ^2=4.301, p=0.038).

From the health and social care perspective, the differences in total costs were not statistically significant, but, from a societal perspective, rehabilitation (combined individual and group) had total costs of £584 more than usual care. Differences in total costs between individual and group rehabilitation were not statistically significant.

For functional improvement, at a willingness-to-pay threshold of £1,900, rehabilitation (both types) had over a 90% probability of being more cost-effective than usual care. At a threshold of £6,000, individual rehabilitation had a probability of only 50% of being more cost-effective than group rehabilitation. For QALYs, at a willingness-to-pay threshold of £19,000, individual rehabilitation had a probability of only 38% of being more cost-effective than either group rehabilitation or usual care.

Authors' conclusions

The authors concluded that rehabilitation, especially group rehabilitation, was cost-effective in the management of chronic knee pain.

CRD commentary

Interventions:

The interventions were clearly reported and the usual care in the authors' setting was used as a comparator, but this was not described.

Effectiveness/benefits:

A randomised controlled trial was an appropriate source for the clinical data, given the strengths of its design. The inclusion and exclusion criteria were reported, but the randomisation methods and power calculations were not. An intention-to-treat analysis was conducted and the patient groups were generally comparable at baseline, making the data more robust. The methods used to handle missing data were appropriate and statistical analysis was used to account for potential biases. The derivation of the benefit measures was reported and the methods were robust. The authors used a disease-specific benefit measure and also reported QALYs, which are a validated measure that allow cross-disease comparisons.

Costs:

The cost categories reflected both the perspectives stated. The resource use was measured using micro-costing methods and the unit costs and resource quantities were reported in an appendix. A detailed breakdown of the cost items was also provided in the paper. Bootstrapping was appropriately employed to determine the mean differences in costs and the estimated 95% confidence intervals. This addressed the problems that can arise from highly skewed cost data. The price year, adjustments for inflation, and the sources of cost data were all well reported.

Analysis and results:

The methods used to synthesise the costs and benefits were appropriate. The issue of uncertainty was thoroughly

investigated and the findings of the base-case and the sensitivity analyses were clearly presented. The authors highlighted some limitations to their study. In general, the reporting was clear and concise, particularly for the costs.
Concluding remarks:
The methods were sound and the study was well reported. The authors' conclusions appear to be appropriate for the scope of their analysis.

Funding
Supported by the Arthritis Research Campaign.

Bibliographic details
Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Williamson E, Jones RH, Reeves BC, Dieppe PA, Patel A. Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. Arthritis and Rheumatism (Arthritis Care and Research) 2007; 57(7): 1220-1229

PubMedID
17907207

Original Paper URL
http://www3.interscience.wiley.com/journal/116324287/abstract

Other publications of related interest
Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Patel A, Williamson E, et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster-randomized trial. Arthritis and Rheumatism 2007; 57: 1211-1219.

Indexing Status
Subject indexing assigned by NLM

MeSH
Adaptation, Psychological; Aged; Aged, 80 and over; Chronic Disease; Cost-Benefit Analysis; Costs and Cost Analysis; Exercise Therapy /economics; Female; Great Britain; Humans; Male; Middle Aged; Osteoarthritis, Knee /economics /physiopathology /rehabilitation; Pain /etiology /prevention & control; Primary Health Care /economics; Quality-Adjusted Life Years; Self Care /economics

AccessionNumber
22007002426

Database entry date
11/08/2010

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain

Jessep SA, Walsh NE, Ratcliffe J, Hurley MV

CRD summary
This study evaluated the feasibility of an integrated community rehabilitation programme and compared its clinical effectiveness and cost-effectiveness in patients with chronic knee pain. The authors concluded that the Enabling Self-management and Coping with Arthritic knee Pain through Exercise (ESCAPE-knee pain) programme was more cost-effective than out-patient physiotherapy, but this needed to be confirmed in a larger trial. The methodology and reporting were satisfactory and the authors' conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the feasibility of an integrated community rehabilitation programme and compared its clinical effectiveness and cost-effectiveness in patients with chronic knee pain.

Interventions
The Enabling Self-management and Coping with Arthritic knee Pain through Exercise (ESCAPE-knee pain) rehabilitation programme was compared with out-patient physiotherapy. The integrated programme combined exercise, patient education, self-management, and coping strategies and was delivered in a community centre.

Location/setting
UK/primary care.

Methods
Analytical approach:
The clinical effectiveness and cost data were derived from a randomised controlled trial (RCT), which compared the ESCAPE-knee pain programme with usual care. The time horizon was 12 months and the authors did not report the study perspective.
Effectiveness data:
The clinical data were derived from a RCT that included 48 people who were followed-up for 12 months after completion of the intervention. Assessment was blind to group allocation. The two groups were comparable at baseline in terms of their prognostic variables and outcome measures. The primary outcome was physical function assessed using the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index. The secondary outcomes were pain, objective functional performance, anxiety, depression, health-related quality of life, exercise-related health beliefs, and health care utilisation.
Monetary benefit and utility valuations:
The health-related quality of life score was assessed, using the European Quality of life (EQ-5D) questionnaire, for each participant at baseline, immediately post-intervention, and at 12 months.
Measure of benefit:
The measure of benefit used to calculate the cost-effectiveness ratio was the EQ-5D utility score.
Cost data:
The cost categories included the intervention costs and knee treatment costs. The resource data were collected prospectively during the clinical trial. Out-patient physiotherapy costs were national reference costs. All costs were in UK pounds sterling (£) and the price year was 2005. No discounting was performed because the time horizon was 12 months.
Analysis of uncertainty:
The authors did not conduct any analysis of uncertainty on the cost-effectiveness results.

Results
Exercise health beliefs were better in the ESCAPE-knee pain group. For all other outcomes, including EQ-5D scores, there were no significant between-group differences.

The total costs were £583 for out-patient physiotherapy and £320 for ESCAPE-knee pain.

The ESCAPE-knee pain programme was more cost-effective and associated with marginally greater improvements in EQ-5D scores, at lower costs, than out-patient physiotherapy.

Authors' conclusions
The authors concluded that the ESCAPE-knee pain programme was more cost-effective than out-patient physiotherapy, but this needed to be confirmed in a larger study.

CRD commentary
Interventions:
The intervention was well described and was appropriately compared with usual care in the clinical setting. These strategies are likely to be relevant in other settings.
Effectiveness/benefits:
The effectiveness data were based on a RCT, which was appropriate for the study question and should have ensured the validity of the clinical analysis. The strengths of the trial included comparable baseline characteristics of the two patient groups and the intention-to-treat approach, but the sample size was small, which contributed to the great uncertainty in the results. The utility data were obtained from the trial, which ensured that the estimates were appropriate for the study population.
Costs:
The authors did not report the perspective, so it is not clear whether the appropriate cost categories were included. The resource use data were obtained from the trial, which ensured the accuracy of these estimates. The authors estimated the costs using national tariffs and national reference costs, which are appropriate sources of cost data. The cost analysis was adequately reported.
Analysis and results:
The use of an incremental analysis was appropriate to determine the cost-effectiveness of the strategies. The authors did not evaluate the uncertainty of their results and this may have been significant given the reported standard deviations. They did acknowledge that their results were uncertain due to the small sample size and they recommended a larger study to confirm them. They also highlighted the strengths and limitations of their analysis.
Concluding remarks:
The methodology and reporting were satisfactory and the authors' conclusions appear to be appropriate.

Funding
Funding received from the Physiotherapy Research Foundation Project.

Bibliographic details
Jessep SA, Walsh NE, Ratcliffe J, Hurley MV. Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. Physiotherapy 2009; 95(2): 94-102

PubMedID
19627690

Original Paper URL
http://dx.doi.org/10.1016/j.physio.2009.01.005

Other publications of related interest
Hurley MV, Walsh NE, Mitchell HL, Pimm TJ, Patel A, Williamson E, et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain; a cluster randomized trial. Arthritis and Rheumatology 2007; 57: 1211-1219.

Indexing Status
Subject indexing assigned by NLM

MeSH
Activities of Daily Living; Aged; Aged, 80 and over; Ambulatory Care /economics; Chronic Disease; Cost-Benefit Analysis; Costs and Cost Analysis; Exercise Therapy /economics; Female; Great Britain; Humans; Male; Middle Aged; Osteoarthritis, Knee /economics /rehabilitation; Pain Measurement; Primary Health Care /economics; Self Care /economics

AccessionNumber

22009103546

Database entry date
27/01/2010

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Cost-effectiveness of aerobic and resistance exercise in seniors with knee osteoarthritis

Sevick M A, Bradham D D, Muender M, Chen G J, Enarson C, Dailey M, Ettinger W H

Health technology
The use of aerobic versus resistance exercise training for patients with knee osteoarthritis.

Type of intervention
Secondary prevention.

Hypothesis/study question
The objective of the study was to investigate the cost-effectiveness of aerobic exercise training and resistance exercise training, compared with a health education programme only. The perspective from which the study was conducted was not stated.

The aerobic exercise training was undertaken three times per week, and consisted of a 3-month facility-based programme and a 15-month home-based programme. The duration of the exercise sessions was 60 minutes. This included the warm-up, stimulus (walking at 50 to 70% of the participants' heart rate reserve), and cool-down phases.

The resistance exercise programme also consisted of a 3-month facility-based programme and a 15-month home-based programme. The duration of the exercise sessions was 60 minutes. The nine exercises performed were leg extension, leg curl, step up, heel raise, chest fly, upright row, military press, biceps curl, and a pelvic tilt. These were designed to strengthen the major muscle groups of both the upper and lower extremities. Beginning with the lowest possible resistance, weight was increased in a step-wise fashion.

The education programme consisted of a monthly 1.5-hour videotaped educational session during the first 3 months, followed by the opportunity to regularly discuss the individual's arthritis status and medications with a nurse.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised individuals aged 60 years or older, with knee osteoarthritis. Individuals were eligible for inclusion in the study if they met the following criteria:

age 60 years or over;

pain on most days of the month in one or both knees;

difficulties with walking quarter of a mile, climbing stairs, getting in and out of a car, rising from a chair, lifting and carrying groceries, getting out of bed or the bathtub, or performing shopping, cleaning or self-care activities, due to knee pain;

radiographic evidence of knee osteoarthritis in the tibial-femoral compartments on the painful knee(s), as judged by a radiologist.

Individuals were excluded from participation if they were seriously ill, they were unable to walk 420 feet in 6 minutes without an assistive device, or they resided in or were planning to move to an extended care facility. They were also excluded if they currently exercised on a regular basis, or were participating in another research study.

Setting
The setting was the community. The economic study was conducted in the USA

Dates to which data relate
The effectiveness and resource use evidence related to a 15-month period from May 1992 to July 1994. The price year was 1994.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
A total of 4,575 individuals were screened by telephone during the study period. Of these, 439 were eligible and agreed to participate in the study. Overall, 144 patients were randomised to the aerobic exercise group, 146 to the resistance exercise group, and 149 to the health education group. The mean age in the aerobic exercise group was 69 (+/-6) years and 31% were men. The mean age in the resistance exercise group was 68 (+/-6) years and 27% were men. The mean age in the health education group was 69 (+/-6) years and 31% were men. No power calculations to determine sample size were reported.

Study design
The study was a single-blind randomised clinical trial carried out in two centres (the University of Tennessee in Memphis and the Wake Forest University at Winston Salem). The duration of follow- up was 18 months. The blinding seems to have referred to the assessment of the outcomes (predominantly self-completed questionnaires). The method of blinding was not reported.

A total of 365 participants (83%) completed the study. The retention was not statistically different among the intervention groups (aerobic group 81%, resistance group 84%, and health education group 83%). The participants who did and did not complete the study were not significantly different in terms of their age, gender, race, number of chronic conditions, initial X-ray score, knee pain or disability score.

Analysis of effectiveness
The basis for the analysis of the clinical study was not stated. It would appear that all the patients included in the study were accounted for in the analysis, thus implying an intention to treat basis. The outcome measures considered in the analysis were self-reported disability, measures of physical performance, and measures of pain frequency and pain intensity on ambulation and transfer.

Self-reported physical disability was measured using an investigator-developed questionnaire of 23 questions, which addressed the amount of difficulty the respondent had with daily activities. Physical performance was determined from the distance walked in 6 minutes, a timed stair climb and descent, a lift and carry task, and the time required to get into and out of a car. The frequency and intensity of knee pain was measured using the Knee Pain Scale (KPS), which was a scale developed in the study and specific to patients with knee osteoarthritis. The four dimensions assessed were transfer pain frequency, ambulatory pain frequency, transfer pain intensity, and ambulatory pain intensity. The groups were comparable in terms of their sociodemographic variables, co-morbid status, and other

health variables.

Effectiveness results
The outcome measures at 18 months were reported for the three groups as follows.

Self-reported physical disability: education 1.90 points, aerobic exercise 1.72 points, and resistance exercise 1.74 points.

Six-minute walking distance: education 1,349 feet, aerobic exercise 1,507 feet, and resistance exercise 1,406 feet.
Stair climb: education 13.9 seconds, aerobic exercise 12.7 seconds, and resistance exercise 13.2 seconds.
Lifting and carrying task: education 10.0 seconds, aerobic exercise 9.1 seconds, and resistance exercise 9.3 seconds.
Car task: education 10.6 seconds, aerobic exercise 8.7 seconds, and resistance exercise 9.0 seconds.
Transfer pain frequency: education 3.18 points, aerobic exercise 2.89 points, and resistance exercise 2.99 points.
Ambulatory pain frequency: education 3.46 points, aerobic exercise 3.12 points, and resistance exercise 3.06 points.
Transfer pain intensity: education 2.28 points, aerobic exercise 2.10 points, and resistance exercise 2.11 points.
Ambulatory pain intensity: education 2.45 points, aerobic exercise 2.27 points, and resistance exercise 2.34 points.

Compared with the health education control group, the aerobic exercise group participants had better scores on the self-reported physical disability, ($p<0.001$), knee pain, ($p=0.001$), 6-minute walking distance, ($p<0.001$), stair climb, ($p=0.05$), lifting and carrying task, ($p<0.001$), and car task, ($p<0.001$).
Compared with the health education control group, the resistance exercise group participants had better scores on the self-reported physical disability, ($p=0.003$), knee pain, ($p=0.02$), 6-minute walking distance, ($p=0.02$), lifting and carrying task, ($p=0.001$), and car task, ($p=0.003$).

Clinical conclusions
The magnitude of the differences in efficiency between the aerobic and resistance exercise programmes, compared with the health education programme, was small when self-reported disability and various measures of physical functions had been analysed.

Measure of benefits used in the economic analysis
No single measure of benefit was used in the economic analysis. However, an incremental cost-effectiveness analysis was carried out for each of the nine outcome measures assessed.

Direct costs
The cost/resource boundary adopted was not explicitly stated. The analysis of the direct costs included:

physician office visits for check-up and consultation on the exercise interventions (1994 Medicare Physician Fee Schedule);

in-centre activities, derived from a survey of local health clubs);

four home visits of the exercise instructor to the exercise participants (based on authors' assumptions);

telephone follow-up (18 follow-up phone calls of 15-minutes each, made by the exercise instructor for the exercise participants and by a nurse for the education participants);

additional medical referrals, due to the detection of physical problems that would otherwise have gone unnoticed (1994 Medicare Physician Fee Schedule), and

the costs associated with adverse events (ICD9 charges).

The unit costs and the quantities of resources were only reported separately for a few items. Discounting was irrelevant since all the costs were incurred over less than two years. The price year appears to have been 1994.

Statistical analysis of costs

No statistical analysis of the costs was carried out.

Indirect Costs
No indirect costs were analysed.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was performed. This assumed a zero probability of adverse events for both exercise groups.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The education programme cost $343.98 per participant. This comprised $171 in in-centre activities, $171 in telephone follow-up, and $1.98 in medical referrals. The aerobic exercise intervention cost $323.55 per participant. This comprised $32.71 in medical consultation, $135 in in-centre activities, $93.25 in home visits, $51.98 in telephone follow-up, $7.95 in medical referrals, and $2.66 in adverse events. The resistance training intervention cost $325.20 per participant. This comprised $32.71 in medical consultation, $135 in in-centre activities, $93.25 in home visits, $51.98 in telephone follow-up, $8.28 in medical referrals, and $3.98 in adverse events.

Both the aerobic and the resistance exercise were cheaper than the education intervention. Compared with the education intervention, the incremental cost of the aerobic intervention resulted in a cost-saving of $20,43 per person and the incremental cost of the resistance intervention in a cost-saving of $18.78 per person. The costing was programme-based for the intervention programme and follow-up.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was carried out, comparing both exercise programmes with the education intervention.

Compared with the education intervention, the incremental costs per incremental unit of improvement with the aerobic intervention were -$114 per self-reported disability score, -$0.13 per 6-minute walking distance, -$17 per stair climb, -$23 per lifting and carrying task, -$11 per car task, -$70 per transfer pain frequency, -$60 per ambulatory pain frequency, -$114 per transfer pain intensity, and -$114 per ambulatory pain intensity.

The corresponding values for the resistance intervention were -$117 per self-reported disability score, -$0.33 per 6-minute walking distance, -$27 per stair climb, -$27 per lifting and carrying task, -$12 per car task, -$99 per transfer pain frequency, -$47 per ambulatory pain frequency, -$110 per transfer pain intensity, and -$171 per ambulatory pain intensity.

The sensitivity analysis, which assumed zero probability of adverse events, had minimal influence on the incremental cost and did not change the conclusions.

Authors' conclusions
Both exercise programmes were cheaper and more effective than a simple education intervention. However, the resistance training for seniors with knee osteoarthritis was slightly more economically efficient than aerobic exercise in improving physical function.

CRD COMMENTARY – Selection of comparators
The authors justified their choice of the education intervention as a comparator on the grounds that is was a means of minimising attention and social interaction biases. You should decide whether the comparator represents current practice in your own setting. The authors acknowledged that other sources of exercise training were available.

Validity of estimate of measure of effectiveness
The analysis used a randomised controlled trial, which was appropriate for the study question. The study sample was

representative of the study population, and the patient groups were shown to be comparable at analysis. The analysis of the clinical study appears to have been conducted on an intention to treat basis, although this was not explicitly stated. The authors stated that the drop-outs were not significantly different from those who remained in the study. Power calculations were not performed.

Validity of estimate of measure of benefit
No summary measure of health benefit was used in the analysis. A number of effectiveness measures were used to derive the cost per unit of effectiveness. The comparisons of the aerobic training and the education programmes, and the resistance exercise and the education programmes, appear to have been inappropriate since both exercise programmes were dominant over the education programme (both more costly and less effective). It would have been more interesting to have compared the two exercise programmes, although the aerobic exercise programme was dominant over the resistance exercise programme in terms of almost all outcomes, with the exception of ambulatory pain frequency.

Validity of estimate of costs
The cost/resource boundary adopted in the analysis was unclear. The major costs and categories were reported. The price year was not reported for the adverse events. Statistical analyses on the quantities were not reported. A sensitivity analysis was only performed for zero probabilities of adverse events for both exercise programmes, and no effect on the final results was observed. The costs and the quantities were reported separately for the occasions where the programme was costed (initial medical visit, in-centre sessions, and follow-up activities). Charges were generally used to proxy prices.

Other issues
The authors made few appropriate comparisons of their findings with those from other studies, and did not address the issue of generalizability to other settings. Thus, the external validity was quite limited. The discussion of the results was limited. The overall authors' conclusion is not justified by the results reported, as the aerobic exercise programme proved to be the most cost-effective intervention, rather than the resistance exercise programme.

Implications of the study
The authors acknowledge that further research is needed to examine the impact of the exercise interventions on the long-term cost and utilisation of health care services, and on the patients' quality of life in terms of general utility.

Source of funding
Supported by the Claude D Pepper Older Americans Independence Center of Wake Forest University, NIH grant number P60AG10484.

Bibliographic details
Sevick M A, Bradham D D, Muender M, Chen G J, Enarson C, Dailey M, Ettinger W H. Cost-effectiveness of aerobic and resistance exercise in seniors with knee osteoarthritis. Medicine and Science in Sports and Exercise 2000; 32(9): 1534-1540

PubMedID
10994901

Original Paper URL
http://www.acsm-msse.com/article.asp?ISSN=0195-9131&VOL=32&ISS=9&PAGE=15 34

Other publications of related interest
Rejeski WJ, Ettinger WH, Shumaker S. The evaluation of pain in patients with knee osteoarthritis: the knee pain scale. Journal of Rheumatology 1995;22:1124-9.

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Community Health Services /economics; Cost-Benefit Analysis; Disabled Persons; Exercise Therapy

/economics; Female; Geriatrics; Humans; Intervention Studies; Knee Joint /pathology; Male; Middle Aged; Osteoarthritis /economics /pathology /rehabilitation; Patient Education as Topic; Weight Lifting

AccessionNumber
22000007671

Database entry date
31/12/2002

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis

McCarthy C J, Mills P M, Pullen R, Richardson G, Hawkins N, Roberts C R, Silman A J, Oldham J A

Bibliographic details
McCarthy C J, Mills P M, Pullen R, Richardson G, Hawkins N, Roberts C R, Silman A J, Oldham J A. Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis. Health Technology Assessment 2004; 8(46): iii-iv, 1-61

PubMedID
15527668

Indexing Status
Subject indexing assigned by NLM

AccessionNumber
22005006103

Database entry date
16/05/2005

Record Status
This is an economic evaluation that meets the criteria for inclusion on NHS EED. If you would like us to consider prioritising the writing of a critical abstract for this economic evaluation please e-mail: CRD-NHSEED@york.ac.uk quoting the Accession Number of this record. Please note that priority is given to fast track requests from the UK National Health Service.

on October 27,2011.

INAHTA Summary

Supplementation of a Home-Based Exercise Program with a Class-Based Program for People with Osteoarthritis of the Knees: A Randomized Controlled Trial and Health Economic Analysis

Aim: To determine if a home exercise program with a class-based program results in greater improvement in walking pain and locomotor function 6 and 12 months after terminating contact with the physiotherapist.

Conclusions and results: At all followups, patients from the supplemented group demonstrated greater improvement in locomotor function and decrease in pain while walking. Pooled estimates of effect were -2.89 seconds (95%CI -1.82 to -3.96) for locomotor function and 14.9 mm (95%CI -11.7 to -18.1) for walking pain, representing between-group differences of 12% and 27% respectively. The supplemented group also demonstrated small, but significant, improvements in balance, strength, WOMAC score, and the physical function and pain dimensions of the SF-36 ($p<0.05$). However, not all of these improvements were maintained over the 12-month followup period. There was no evidence that adherence to the home exercise program differed between the groups, although the supplemented group noted an increase in their physical activity. There was no evidence that mean QALY gains differed significantly between the groups. However, costs were slightly lower and QALY gains slightly higher in the group with the supplementary class-based program. Thus, for most reasonable values of a decision maker's willingness-to-pay for an additional QALY, adding a class-based program is likely to be cost effective. There was considerable uncertainty around this estimate, with a probability of 30% to 35% that the intervention was not cost effective.

Recommendations: Supplementing a home-based exercise program with a class-based exercise program led to superior improvement in the supplemented group. These clinically important improvements were still evident at review 12 months after treatment had ceased. The additional cost of the supplemented group was offset by reductions in resource use elsewhere in the system. Adherence to the home exercise program did not differ between the groups at the 6- and 12-month assessments, despite considerable difference in the intensity of the two treatments.

Methods: The trial was a pragmatic, single-blind, randomized clinical trial accompanied by a health economic assessment. Patients were randomly allocated to either home or home supplemented with class exercise programs. Both groups were given a home exercise program aimed at increasing lower limb strength, endurance, and improving balance. The supplemented group also attended knee classes by a physiotherapist, twice weekly for 8 weeks. Classes represented typical knee class provision in the UK. Assessments of impairment, disability, and handicap were made pretreatment, posttreatment, and at 6 and 12 months posttreatment. Analysis involved the use of a longitudinal linear model, ANCOVA. The economic evaluation looked at utilization of health service resources

and assessed cost effectiveness by relating differential costs to differences in quality-adjusted life-years (QALYs) based on patients' responses to the EQ-5D.

Further research/reviews required: Future research should investigate methods of increasing adherence with home exercise and evaluate the interventions in the primary care setting.

Written by: Dr Christopher J McCarthy, Central Manchester Healthcare Trust, United Kingdom

Cost effectiveness of a two-year home exercise program for the treatment of knee pain

Thomas K S, Miller P, Doherty M, Muir K R, Jones A C, O'Reilly S C

Health technology
Non-medical interventions for knee osteoarthritis (OA) were examined. These were exercise therapy, monthly telephone contact, and a combination of exercise therapy and telephone contact.

The exercise programme comprised quadriceps strengthening and aerobic exercise taught in a graded programme. Resistance exercises were taught using rubber exercise bands. A research nurse taught the programme in the participants' homes. The initial training phase consisted of 4 visits lasting approximately 30 minutes in the first 2 months, with follow-up visits scheduled every 6 months thereafter. The participants were encouraged to perform the programme daily, taking 20 to 30 minutes to do so.

Monthly telephone contact was used to monitor symptoms and to offer simple advice on the management of knee pain. This intervention aimed to control for the psychosocial contact of the exercise programme. The calls typically lasted 2 minutes (8 minutes for the first call), although the time spent on the administration of calls was considerably more (more than 4 times).

Type of intervention
Treatment.

Hypothesis/study question
The objective of the study was to assess the cost-effectiveness of exercise therapy, monthly telephone contact, and both exercise therapy and telephone contact in comparison with no intervention for the treatment of knee OA in the UK. The participants in the no-intervention control group received no contact between the biannual assessment visits. The authors stated that studies had shown that exercise therapy could reduce the symptoms of knee OA. However, little was known about the cost implications of delivering such an intervention. The current pharmacoeconomic study was based on the clinical results of a published randomised trial (Thomas et al. 2002, see 'Other Publications of Related Interest' below for bibliographic details). The authors stated that the perspective of the National Health Service (NHS) and the patient was adopted in the study.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients reporting current knee pain. The exclusion criteria were total knee

replacement, lower limb amputation, cardiac pacemaker, unable to give informed consent, or no current knee pain.

Setting
The setting was primary and secondary care. The economic study was carried out in the UK.

Dates to which data relate
The clinical evidence and resource use data were derived from a study published in 2002. The price year was 1996.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The patients were identified from a postal questionnaire of 9,296 people aged at least 45 years who were registered at two general practices in Nottingham. Of these, 3,261 did not respond and 4,103 were knee pain negative. Of the 1,932 who were knee pain positive, 295 refused to participate, 327 were excluded, and 464 were unable to be contacted. A further 60 patients were excluded or refused to participate. Thus, a group of 786 patients was included in the final study sample and allocated to the different groups. The mean age of the participants was 62 years, and 64% were women. There were 235 patients in the exercise plus telephone group, 235 in the exercise group, 160 in the telephone group, and 156 in the placebo or no intervention group. It was not stated whether any power calculations were carried out in the primary study.

Study design
This was a prospective, randomised clinical trial that was carried out at two general practices in Nottingham. The participants were randomised using a computer-generated list with a block size of 10, and stratified by age and gender. To limit the number of dropouts in the trial, participants allocated to the no-intervention control group and the combined exercise and telephone group were further randomised to receive or not receive a placebo health food tablet. However, given that no differences were found between the groups receiving or not receiving the placebo health food tablet, all analyses were presented according to the original design. The length of follow-up was 2 years. Data were not available for 27 patients (9 in the exercise plus telephone group, 9 in the exercise group, 6 in the telephone group and 3 in the placebo group) who were then excluded from the primary analysis. However, the authors stated that these patients were comparable, in terms of their age and gender, to those whose follow-up data were available.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary effectiveness measure was a clinically significant improvement in knee pain (>/= 50%) at 24 months, measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The authors stated that the study groups were comparable at baseline.

Effectiveness results
Both the exercise and no-exercise groups had reduced WOMAC pain scores at 2 years. This improvement was significantly greater in the exercise groups than in the no-exercise groups (mean change compared with no exercise -0.74, 95% confidence interval, CI: -1.22 - -0.25; p=0.003).

Similar improvements were not observed for the telephone groups compared with the no-telephone groups (mean change compared with no telephone -0.19, 95% CI: -0.67 - 0.29; p=0.44), and no interaction between exercise and telephone was seen, (p=0.72).

One hundred and twenty (27%) participants allocated to receive exercise therapy showed an improvement of at least 50% in knee pain compared with 62 (20%) participants allocated to the non-exercise groups, (p=0.1).

Ninety-one (24%) participants allocated to the telephone group showed an improvement of at least 50% in knee pain compared with 91 (24%) participants allocated to no telephone, (p=0.87).

Clinical conclusions
The effectiveness analysis showed that the mean improvements in knee pain were significantly better in the exercise group than in the no-exercise group, while no significant differences were found between the telephone and no-telephone groups.

Measure of benefits used in the economic analysis
The summary benefit measure used was the proportion of patients achieving at least a 50% improvement in knee pain. This was derived directly from the effectiveness analysis.

Direct costs
The cost analysis was performed from the perspective of the NHS and the patient. The costs of the interventions, medical costs (secondary and primary care costs) and personal costs (costs incurred by the patient in accessing health services) were included. In particular, intervention costs included start-up and ongoing costs for both exercise and telephone, while long-term costs included the general practitioner (GP), GP-prescribed drugs and secondary care costs. A detailed breakdown of the cost items was provided. The unit costs were presented separately from the quantities of resources used. The costs were estimated using the Personal Social Services Research Unit, the local hospital finance department, and the British National Formulary. The resource use data were derived from the sample of patients included in the effectiveness study, after excluding 27 patients for whom data were not available. Two patients incurred very high medical costs, thus the economic results were presented both with and without these patients. The costs that were incurred in the second year were discounted at a rate of 5%. The price year was 1996.

Statistical analysis of costs
A non-parametric bootstrapping approach was used because of the skewed distribution of the cost estimates. Two thousand re-sampled estimates were calculated. Statistical tests were also performed to test the statistical significance of differences in the costs.

Indirect Costs
The indirect costs were not considered in the economic analysis.

Currency
UK pounds sterling ().

Sensitivity analysis
A univariate sensitivity analysis was performed to assess the impact of variations in personnel costs on the estimated cost-effectiveness ratios. In particular, the analysis was run using physiotherapy assistant costs that were lower than those used in the base-case. The analysis was also replicated using sub-groups of patients, such as those who presented to their GP, non-obese patients, and those with no radiographic evidence of OA.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The costs were estimated for the exercise programme (which included both the exercise group and the exercise plus telephone group) versus the no-exercise programme (which included both the telephone group and the placebo group).

The intervention costs to the health care provider for the 2-year period were 112 per person for the exercise programme and 61 per person for the telephone intervention.

The average total costs per patient were 1,358 (+/-1,962) (95% CI: 1,177 0 1,539; median 698; interquartile range, IQR: 1,021) for the exercise intervention (exercise plus exercise with telephone support groups; n=451) and 1,128 (+/-1,512) (95% CI: 989 - 1,268; median 588; IQR: 1,050) for the no-exercise control (telephone support plus no intervention groups; n=306). The difference was not statistically significant, (p=0.08).

After bootstrapping adjustment, the average total costs per patient were 1,354 (+/-91) (95% CI: 1,350 - 1,358; median 1,351; IQR: 119) for the exercise intervention and 1,129 (+/-84) (95% CI: 1,125 - 1,132; median 1,128; IQR: 115) for

the no-exercise control. The difference reached statistical significance, (p=0.001).

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (i.e. the incremental cost per clinically significant improvement) was calculated to combine the costs and benefits of the interventions examined in the study.

The incremental cost per a clinically significant improvement with exercise in comparison with no exercise was 2,570. Cost-effectiveness acceptability curves showed that if decision-makers were prepared to pay 8,000 for each patient showing at least a 50% improvement in knee pain, the probability that the exercise intervention would be cost-effective was very high. However, if health providers were only willing to pay less than 500, it was almost certain that it would not be cost-effective.

The sensitivity analysis showed that the cost-effectiveness ratio would have fallen to 2,090 when incorporating physiotherapy assistant costs and to 814 if the analysis was restricted only to patients who presented to their GP. Even better cost-effectiveness ratios were achieved in the sub-groups of non-obese patients and those with no radiographic evidence of OA.

Authors' conclusions
Exercise therapy provided significant health benefits for individuals with knee pain, but the cost of delivering the exercise programme was not offset by any reduction in medical resource use. Thus, the cost-effectiveness of the intervention depends on the decision-makers' willingness to pay.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. The interventions examined in the study were described. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. The trial had been published already, but extensive details on the methods of sample selection and randomisation were given. The numbers of patients refusing to participate or excluded from the study sample were reported, although the authors did not report the reasons for such refusals. The internal validity of the study was further ensured by the baseline comparability of the study groups and the use of intention to treat analysis. The length of follow-up was appropriate. The study sample appears to have been representative of the patient population. It was not stated whether power calculations were carried out to justify the size of the sample.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It is not comparable with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs was consistent with the perspective adopted in the study. The authors noted that the inclusion of indirect costs would have been interesting. The unit costs and quantities of resources used were reported extensively, which would help replication of the study in other settings. Discounting was relevant for some costs incurred in the second year. The source of the data was reported. Statistical analyses were performed to deal with the skewed distribution of the costs. Further, a sensitivity analysis was carried out on a key cost estimate. The price year was reported, which aids reflation exercises in other time periods.

Other issues
The authors reported the results of some US studies (that reported small savings associated with exercise therapy) and some UK studies (which showed little or no benefits associated with exercise therapy). Several sub-group analyses were performed, which enhanced the applicability of the study results. However, the issue of the generalizability of the study results to other settings was not explicitly addressed and limited sensitivity analyses were performed. This reduces the external validity of the analysis. The study referred to patients with knee pain and this was reflected in the authors' conclusions.

Implications of the study

The study results showed some sub-groups of patients who may benefit from the exercise programme at a cost affordable to the NHS. Future studies should be carried out to better identify such patients.

Source of funding
None stated.

Bibliographic details
Thomas K S, Miller P, Doherty M, Muir K R, Jones A C, O'Reilly S C. Cost effectiveness of a two-year home exercise program for the treatment of knee pain. Arthritis and Rheumatism (Arthritis Care and Research) 2005; 53(3): 388-394

PubMedID
15934131

Other publications of related interest
Thomas KS, Muir KR, Doherty M, et al. Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. BMJ 2002;325:752-7.

Sevick MA, Bradham DD, Muender M, et al. Cost-effectiveness of aerobic and resistance exercise in seniors with knee osteoarthritis. Med Sci Sports Exerc 2000;32:1534-40.

Barlow JH, Turner AP, Wright CC. Long-term outcomes of an arthritis self-management programme. Br J Rheumatol 1998;37:1315-9.

Lord J, Victor C, Littlejohns P, et al. Economic evaluation of a primary care-based education programme for patients with osteoarthritis of the knee. Health Technol Assess 1999;3:1-55.

Indexing Status
Subject indexing assigned by NLM

MeSH
Cost-Benefit Analysis; Exercise Therapy /economics; Female; Home Care Services /economics; Humans; Knee; Male; Middle Aged; Osteoarthritis, Knee /therapy; Outcome Assessment (Health Care); Pain /economics /therapy

AccessionNumber
22005006396

Database entry date
28/02/2006

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Appendix 2.4 Excluded studies

Study	Reason for exclusion
Unknown Author,. 2010	Acupuncture intervention
Unknown Author, .2010	No OA intervention
Unknown Author,. 2009	Only discusses drugs
Unknown Author, 2008	No OA intervention, only discusses obesity
Unknown Author, 2007	No OA intervention, only discusses weight-loss interventions
Abbott, J.H. 2009	Only a protocol, no results
Abdelhafiz, A.H. 2002	Not a RCT, no aerobic exercise program
Ade, A. 2010	Not a RCT, no aerobic exercise program
Adya, C.M. 2002	Only discusses drugs
Aglamis,B. 2009	Only has SF-36 and WOMAC results, no economic or resource utilization
Aglamis,B. 2008	Only has SF-36 and WOMAC results, no economic or resource utilization
Ahmadi, 2010	No OA intervention
Akyol, 2010	No economic information
Al Mukaimi, A. 2008	Only discusses knee anthroplasty as intervention
Alarcon, G.S. 1995	Only discusses drugs
Alexandre. A, 2010	Not a OA intervention
Allen, K.D. 2008	No aerobic exercise program
Almeida, G.J, 2010	Not a OA intervention
Altay,F., 2010	TENS vs exercise
Altman, R.D. 2009	Drug intervention
An, B. 2008	No aerobic exercise intervention, Baduanjin intervention,
Anderson, P. 2009	Does not discuss OA, only obesity
Andrews, G. 2006	Combines medication with exercise
Argoff,C., 2010	Opiod intervention, non-OA
Artham, S.M. 2010	Does not discuss OA, only obesity
Ashworth,N, 2005	No OA aerobic exercise intervention
Atamaz,F. 2006	Compares drugs with (PTA) physical therapy agents
Babacan,B. 2001	Bracing intervention
Bagga,H. 2003	Hyaluronic acid intervention
Baker, K. 2007	Insole treatment intervention
Baker, K.. 2000	Systematic review of exercise for knee OA
Baker, K.. 2001	Strength training program, SF-36 information
Bales, C.W. 2008	Weight loss intervention, no economic information
Balint,G. 1995	No aerobic exercise intervention, no economic information
Banning,M. 2005	Not an RCT, no aerobic exercise intervention
Barbagallo,M. 2003	Not an RCT
Barlow, J.H. 2000	Self-management Education program
Barondess, J.A. 2008	No RCT, no economic information
Bartels, E.M. 2007	Aquatic exercise intervention
Barton, G.R. 2008	Exercise and diet advice intervention
Baum, K., 2009	Does not discuss osteoarthritis, no economic information.
Bean, J.F., 2004	Not an RCT, no economic information
Beaudreuil, J., 2009	CPG for knee sleeves, knee braces etc
Beaupre, L.A. 2001	Intervention following knee arthroplasty
Beaupre, L.A. 2004	Discusses QOL and health care utilization following knee arthroplasty
Belcaro, G. 2008.	Only discusses drug intervention
Belza, B. 2002	No economic information, aquatic exercise intervention

Bennell, K.L., 2004	No economic information
Bennell, K. L, 2010	Physiotherapy for hip OA
Bennell, K.L, 2011	Systematic review OA exercise interventions, no specific OA economic information
Bergland, A	Exercise and osteoporosis
Beverly, C. 2001	Cost and exercise information, but no economic evaluations
Biligici, A., 2005	Article not in English, does not appear to have economic information
Bischoff, H.A., 2003	No economic information
Blanchard, C., 2004	Hip OA, HU12, HU13 health utilities index
Boardman, D.L. 2000	Hip OA
Bonnin,M.P., 2009	Ankle arthroplasty
Boon, A.J., 2010	Only discusses drugs
Bork, H., 2005	German, self help education, no economic
Bowman, M.A., 1993	No OA, no economic information
Bradley, J.D., 2000	Not an RCT, no economic information
Brady,T.J.	Provides information on costs of exercise programs but no economic evaluations
Brander,V.A., 1997	Hip and knee arthroplasty
Brandt, K.D., 2003	Only discusses drugs
Braun, L., 2008	No aerobic exercise program. Uses acupuncture and alternative medicine
Brooks, P.M., 2006	No aerobic exercise intervention
Brooks, P.M., 2004	No aerobic exercise intervention, no economic information
Brooks,P.M., 2002	No aerobic exercise intervention but has economic information
Brouwer,R.W., 2006	Brace intervention
Brukner,P.D., 2006	No aerobic exercise intervention
Bruyere, O., 2009	Not a RCT, no economic information
Buchner,D.M, 1997	Not an RCT, no OA intervention
Bulthuis, Y., 2007	Aerobic exercise intervention but no economic information
Bulthuis, Y., 2008	Economic information, intervention is post-surgery
Bunning, R.D., 1991	No economic information, no aerobic exercise intervention
Buskila,D., 2009	Only discusses fibromyalgia
Buskila D, 2009	Only discusses fibromyalgia
Cadmus,L., 2010	Aquatic exercise program
Cakmak, A, 2010	Osteoporosis intervention
Castaneda,D.M., 1998	Not a specific aerobic exercise intervention, only a surveyed trial
Celiker,R., 2009	In Turkish, can't access it
Cevei.M, 2010	Osteoporosis and disability
Chaiprinyo, K., 2009	No aerobic exercise intervention, no economic information
Chaput,J.-P., 2005	No OA, focuses on obesity
Card, J., 2002	No aerobic exercise, no economic information
Chen,D.-Y.,2007	No aerobic exercise intervention, no economic information
Chen,Y.-Y., 2005	Article is in Mandarin, does not appear to be any economic information.
Cheon,E.Y., 2005	Article in Korean, does not appear to be any economic information
Chodzko-Zaiko,W.J., 2009	No aerobic exercise intervention
Chou,C.-W., 2009	Only discusses drugs
Chou,R., 2008	No OA aerobic exercise intervention
Choy, M., 2007	Only discusses drugs
Chrubasik,S.,2004	Only discusses drugs
Chrubasik,S., 2003	No OA aerobic exercise intervention, no economic information
Clark, K.L., 2007	Nutrition intervention
Clarke, A.K., 1999	Not a RCT, no aerobic exercise OA intervention

Cochrane, T., 2005	Aquatic- based therapy
Coleman, S., 2008a	Self management intervention , how to exercise, contains SF36 scores
Coleman, S., 2008 b	Self management intervention with exercise
Cook,C., 2007	Telephone survey regarding exercise and QOL
Corradini, C, 2010	Femoral neck fractures
Cosiales,P.B., 2010	Weight loss intervention
Coulter,C.L., 2009	Group physiotherapy after arthroplasty
Coupé, 2007	Behavioural intervention, not enough detail on exercise intervention
Dalbeth N, 2008	Not an RCT commentary on various OA interventions
Daly,M.P., 1993	No economic. Information but has information on exercise
Davenport,G., 2004	No OA aerobic exercise intervention
Dawson,J., 2007	Foot surgery intervention
De Souza,R.F., 2008.	Temporomandibular joint osteoarthritis
Desmeules,F., 2009	Telephone interview, no OA aerobic exercise intervention
Dias,R.C., 2003	Contains an OA aerobic exercise intervention with SF36 scores but no economic information
Dillard,J.N., 2005	No OA aerobic exercise intervention
Dionyssiotis	Exercise and osteoporosis
Diracoglu,D., 2005	No OA aerobic exercise intervention
D'Lima, D.D., 2005	No OA aerobic exercise intervention
Doi, T., 2008	No OA aerobic exercise intervention
Dowdy,P.A., 1998	No economic information
Dugan,S.A., 2008	Exercise for childhood obesity
Dunbar-Jacob, J, 2005	Not an RCT, discusses various co-morbid conditions
Dunn, A. R.,2010	No economic information
Dureja,H, 2003	No OA intervention, neutraceuticals
Duwelius,P.J., 2008	Hip arthroplasty intervention
Ebert,J.R., 2008	Matrix-induced autologous chondrocyte implantation(MACI) intervention
Elrawady,F., 2005	Not an RCT, no OA intervention
Emery,P., 2008	Only discusses drugs
Epstein,B.J., 2009	Not an RCT, no OA aerobic exercise intervention
Ericsson, Y.B	Menisectomy intervention
Ernst,E., 2007	Massage intervention
Ertekin, C, 2010	Lumbar spinal stenosis intervention
Evcik,D., 2002	OA aerobic exercise intervention but not economic information, contains NHP scores (QOL)
Eyigor,S., 2004	Isokinetic and progressive resistive exercise(PRE) intervention
Farcas, D. 2010	Exercise and osteoporosis
Fary,R.E., 2009	Pulsed electrical stimulation intervention
Fernandes, 2009	Hip OA patient education program
Ferrara,P.E.,2008	No economic information
Fiechtner, J.J.,2002	Manual manipulation intervention, no economic information
Fitzcharles, M, 2010	Drug intervention
Focht, B.C., 2006	OA aerobic exercise intervention but no economic information
Foley,A, 2003	Hydrotherapy intervention
Forestier,R., 2010	Spa therapy treatment intervention
Fransen,M., 2001.	Electrophysical therapy intervention

French,H.P.,2009	Strengthening exercises and stretching intervention OA of hip
Fuchs,S.,2003	Ankle athrodesis
Galea,M.P., 2008	Exercise after hip replacement
Geenen.R, 2010	Psychological intervention
Glasgow,A.C.A, 2002	Only discusses drugs
Gobbi.A, 2010	Tissue engineering intervention
Goodwin,J.L.R., 2005	Opioid treatment
Gorevic, P.D., 2004	Not an RCT, no economic information
Goucke,R., 2009	No OA aerobic exercise intervention
Graham,H.K., 2002	No OA aerobic exercise intervention, cerebral palsy
Grahame,R.,2001	No OA aerobic exercise intervention, hypermobility
Gregg, E.W. 2002	Non-OA intervention, diabetes incidence
Grindrod,K.A.,2010	RCT with no control group, no specific aerobic exercise intervention
Grober,J.S.,2003	Not an RCT, only describes OA
Gunnarsson,O.T., 1997	Does not describe OA, only exercise
Gur,A., 2003	Laser therapy
Haltiwanger,E.,2009	Occupational therapy, no OA aerobic exercise intervention
Hanada,E., 2003	Not an RCT, no OA economic information
Hanypsiak, B.T., 2005	Only discusses drugs
Harper,A., 2003	Does not discuss OA
Heath,J.M., 2002	Not an RCT, discusses exercise for OA but no economic information
Herrlin,S.,2007	Arthroscopic treatment for meniscus tears
Herron,M.L.,2006	Ankle interventions
Hicks,G.S.,2002	Does not discuss OA, back pain
Hinman,R.S, 2007	Aquatic exercise intervention, no economic information
Hinman,R.S.,2008	Insole intervention
Hochberg,M.C., 2007	No exercise and economic information
Hoeksma,H.L., 2004	Hip OA
Holla, J., 2009	Discusses multiple interventions for OA including exercise (aerobic exercise) but no economic information
Hollmann,W.,2007	Not an OA intervention
Holman,H.R., 1997	Not an RCT but may have relevant information about OA
Holtzman,J.,2002	Hip arthroplasty intervention
Hoogeboom, T.J., 2010	Exercise intervention prior to hip replacement.
Hopman-Rock,M.,2000	No costs
Huang,M.H.,2005	Isokinetic exercise intervention, no economic information
Hughes,S.L.,2006	OA aerobic exercise program but no economic information
Hunter,D.J.,2008	Not a RCT but discusses various OA interventions
Hunter.D.J, 2010	Review of OA intervention, no costs
Hurley,M.,2007	Not specific to OA, no economic information
Hurley,M.V.,2009	Not an RCT
Hurley, M., 2009 b	No economic information
Hurley. M, 2010	No economic information
Husby.V.S.,2010	Postoperative hip arthroplasty intervention
Hussey,J.,2003	Not an RCT, no OA aerobic exercise intervention
Ibanez,A.E.,2008	Total knee anthroplasty, rehabilitation intervention

Ike,R.W.,1989	No economic information
Issy, 2005	Article in Portuguese
Issy,A.M.,2005	No OA aerobic exercise intervention, discusses drugs and other interventions for musculoskeletal disorders
Iudica, 2000	Physical therapy and exercise intervention, shows cost of intervention, no resource or QOL information
Jelsma,J.,2002	No OA aerobic exercise intervention, discusses multiple chronic conditions
Jonson,J.E.,2009	Not an RCT
Jorge, 2010	No economic information
Jourdan, 2010	Hip arthroplasty, no economic information
Juul-Kristensen, 2010	No OA intervention, no economic information
Kamer,L.,2009	Only discusses obesity and diabetes
Kang, W, 2009	Abstract, no aerobic exercise intervention
Karacabey,K.,2005	Only discusses exercise in general, no OA aerobic exercise intervention
Karmali,S.,2005	Surgery intervention for obesity
Karmisholt,K.,2005	No specific OA aerobic exercise intervention, Systematic review of exercise for various health conditions
Kauppila,A.-M.,2009	No OA aerobic exercise intervention, just discuses correlation of disability and OA
Keener,J.D.,2003	Hip arthroplasty intervention
Kemper, 2004	Overweight and obesity, no economic information.
Kerr,R.G.,2001	No economic. Information
Kettunen,J.A., 2004	Not a RCT, systematic review of exercise and OA
Kilic,E.,2009	QOL after knee arthroplasty
Kim, 2010	QOL information on OA
Kirane, 2010	Bracing intervention, no economic information
Kirpikova,M.N.,2008	Educational interventions, no OA aerobic exercise intervention
Kirchner,S.,2003	Hip OA, hip arthroplasty
Koybasi, 2010	Hip OA, ultrasound intervention
Ksibi,I., 2008	No economic information
Kuptniratsaikul,V., 2007	No OA aerobic exercise intervention
Kuptniratsaikul, V., 2002	No economic information
Kuritzky,L., 2003	Only discusses drugs
La Croix,A.Z.,1997	No OA aerobic exercise intervention, not an RCT
LaBella, 2010	No OA, knee ligament injuries interventions
Lange,A.K.,2007	No OA aerobic exercise intervention
Lange,A.K.,2008	Strength training, not an RCT, a systematic review but has economic information
Lange,A.K.,2009	Strength resistance intervention. No economic information
Laskin,R.S.,1999	Total knee replacement
Laskowski,E.R.,2009	Obesity intervention
Laupacis,A.,1993	Hip replacement
Lee,H.,2009	Tai Chi Quigong intervention
Lee,Y.C., 2008	Not an RCT, no aerobic exercise OA intervention
Legovic,A, 2006	Knee arthroplasty intervention
Lems, 2010	Not an RCT, no economic information
Leonardi, 2006	Spinal disorders, pharmacological intervention

Li, 2006	Article in Korean, does not appear to have con information.
Liebs, 2010	Cycling intervention after hip, knee replacement
Lim, 2010	Aquatic exercise, no economic information
Lin, 2010	Pharmacological intervention
Lin, 2001	No exercise intervention, no economic information
Ling, 2010	Drug survey for OA no exercise intervention
Lippi, 2006	Not an RCT, no economic information
Liu, 2009	No OA information
Logue, 2010	Obesity outcome,
Lopez-Olivo, 2010	Knee arthroplasty QOL
Lorig, 2008	Self-management intervention, no economic information
Loudon, 2003	Not an RCT, no economic information
Lydell, 2005	No OA knee outcome, no economic information
M.Jolles, 2006	Hip arthritis, arthroplasty intervention
Maddali, 2010	No economic information
Mahon, 2002	No exercise intervention
Maly, 2006	No exercise intervention. No economic information
Mandell, 2001	No exercise OA inter, not RCT, no economic information
Manek, 2001	No economic information
Manskey, 2006	Tai chi intervention, no OA outcome
March, 2010	OA guidelines, no economic information
Marks, 2001	No economic information
Martin, 2007	Pharmacological intervention
Maurer, 1995	Only looked at cost-effectiveness of recruitment methods
May, 2010	No economic information
Mazzuca, 2004	Pharmacological intervention
McCarberg, 2001	No economic information
McNair, 2009	OA of the hip
McNeill, 2011	No economic information, information on treatment options
Meisler, 2002	Not an RCT, no economic information
Meisler, 2001	Not an RCT, no economic information, RA
Mernitz, 2004	No OA or economic information
Messer, 2007	No OA information
Middleton, 2009	Lumbar spondylosis, non-OA outcome
Mikkelsen, 2010	Hip-replacement outcome
Miller,2003	Economic evaluation protocol
Miller 2002	Weight management intervention
Minns Lowe, 2007	Post knee arthroplasty
Minns Lowe, 2009	Post hip arthroplasty
Miszko, 2000	No OA intervention
Miyahara, 2010	No OA intervention
Momani, 2002	Pharmacological intervention
Moseley, 2009	Surgery intervention
Moskowitz, 2003	Pharmacological intervention
Muraki, 2010	No economic. information

Murphy, 2007	No economic. information
Neto, 2010	After kne arthroplasty
Nguyen, 2007	Surgery intervention, no economic information
Nicolakis, 2002	Non-OA outcome, myofascial pain dysfunction syndrome
Nunez, 2010	Post surgery intervention
Nunez, 2006	Educational intervention
Nyland, 2007	Post surgery intervention
Omori, 2005	No economic information, summary of various historical knee OA trials
Omran, 2010	Osteoporosis outcome
O'Reilly, 2001	No economic information
Osborne, 2007	Educational intervention
Overdevest, 2010	Lumbar stenosis outcome
Paans, 2009	Hip OA
Page II, 2008	Pharmacological intervention
Pal, 1993	Pharmacological intervention
Parmelee, 2007	Association of pain and physical disability with depression
Patrick, 2001	Aquatic exercise intervention
Pedersen, 2006	No economic information
Peloquin, 1999	No economic information
Penninx, 2001	No economic information
Peter, 2010	No economic information
Petrella, 2006	Pharmacological intervention
Petterson, 2007	Knee arthroplasty
Petursdottir, 2010	No economic information
Piechota, 2005	Obesity outcome
Pisters, 2010	No economic information
Pittler, 2010	Water therapy, no economic information
Porcheret, 2007	No economic information
Premaor, 2010	Osteoporosis outcome
Provelengios, 2010	Foot deformity outcome
Przekop, 2010	Neurocognitive intervention
Rakicioglu, 2006	Diabetes outcome
Rao, 2004	No OA information
Reilly, 2001	Hydrotherapy intervention
Rejeski, 1997	No economic information
Rejeski, 2002	No economic information
Rissanen, 1999	No economic information
Roine, 2009	Systematic review of Economic eval for OA
Rorabeck, 1994	Hip arthroplasty
Rosemann,2008	No economic information
Rosemann,2005	No economic information
Roy, 1996	No exercise intervention, no economic information
Rubin, 2005	Pharmacological interventions
Russell, 2011	Post knee arthroplasty intervention
Rydevik, 2010	Hip OA

Sanchez, 2010	Assistive device intervention
Sarzi-Puttini, 2010	Fibromyalgia outcome, endocrine therapy
Savelkoul, 2003	Systematic review of self-management interventions
Scanzello, 2008	Pharmacological intervention
Schilling, 2003	No economic information
Schmitz, 2010	No economic information
Schumacher, 2004	No economic information
Scott, 1973	Contains information on costs but is dated
Segal, 2004	Contains cost/QALYs for various interventions including exercise
Sevick, 2009	Diet and exercise among obese individuals
Shahady, 2000	No economic information
Shahcheraghi, 2007	Tibial valgus osteomy outcome
Sharkey, 2000	No economic. information
Shen, 2008	No OA information
Shen, 2009	Knee arthroplasty intervention
Simpson, 2006	No economic. information
Sluka, 2003	Trans. Electrical nerve stimulation intervention
Sokka, 2008	No economic. information
Solignac, 2004	No economic. information
Stebbing, 2010	Fatigue outcome
Steinmeyer, 2006	Oral treatment intervention
Stitik, 2008	Pharmacological intervention
Stitik, 1999	No economic. Information.
Stolwijk-Swuste, 2008	Poliomyelitis outcome
Stove, 2005	Not in English
Strobl, 2001	Cerebral palsy outcome
Suggs, 2009	Pharmacological intervention
Sun, 2007	No OA information
Sutbeyaz, 2007	Quality of life among obese, no economic, information
Svege, 2010	Hip OA
Svetlova, 2010	No economic. information
Tak, 2005	Hip OA
Tamari, 2010	No OA economic information
Tan, 2010	No OA economic information
Thapar, 2004	No OA economic information
Thorlund, 2009	No OA economic information
Thorstensson, 2005	No economic information but good exercise information
Tilden, 2010	No economic information.
Tohyama, 2010	No economic information
Tosi, 2000	Surgery intervention
Totorean, 2010	No economic information
Towheed, 2002	Pharmacological intervention
Traistaru, 2010	No economic information
Tsai, 2004	No economic OA information
Tugwell, 2001	No economic information

Tuzun, 2007	No economic information
Underwood, 2004	No specific OA costs
Vaarbakken, 2007	Hips disability outcome
Vad, 2002	Exercise and pharmacological intervention
Vad,2004	No OA information
Van De Koppel. 2008	Diabetes outcome
Vasic, 2010	Osteoporosis outcome
Veale, 2007	No OA information
Verbeek, 2009	Comment on Jessep et al. 2009
Vo , 2009	No cost-effectiveness analysis but has economic and OA information
Vondracek, 2010	Osteoporosis outcome
Vuori, 1998	No OA information
Vynios, 2005	Pharmacological intervention
Waddell, 2007	Pharmacological intervention
Walker, 2002	Surgery intervention
Walker-Bone, 2003	No economic information
Walls, 2010	Electrical stimulation intervention, knee arthroplasty
Wang, C, 2008	Tai chi, no economic information given
Wang, J.L, 2008	No economic information
Wang, T.M., 2005	No economic information
Wenham, 2010	Acupuncture and pharmacological intervention
Westby, 2009	Hip arthroplasty
Westy,2006	No economic information
Whitehurst, 2009	Acupuncture intervention
Williams, 2009	Design of economic evaluation protocol
Williamson, 2007	Costs but no resource utilization given
Witham, 2010	Weight loss intervention, obesity outcome
Wong, 1999	Hip arthroplasty
Wright, 2010	Knee arthroplasty
Wu, 2005	Has information on exercise and OA but no economic information
Yager, 2005	Heart failure outcome
Yilmaz, 2010	No economic information
Ying, 2007	TENS intervention
Yoo,2011	Knee arthroplasty
Yurtkuran, 2007	Acupuncture intervention
Yurtkuran, 2006	Balneothreapy intervention
Zacher, 2002	Pharmacological intervention
Zhang, 2007a	Hand OA
Zhang, 2008	No economic information for exercise
Zhang, 2007b	No economic information for exercise but valuable systematic review information on aerobic exercise
Zhang, 2010	Systematic review of OA cost effective interventions
Zheng, 2006	Pharmacological intervention
Zoran, 2010	Animal subjects

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Unknown Author. Acupuncture.Focus on Alternative and Complementary Therapies.2010;15(2):163-69

Unknown Author. Other complementary therapies. Focus on Alternative and Complementary Therapies;2010:15(2):175-179.

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Appendix 3.1 Post-Randomization Walking Interventions

		INDIVIDUAL AEROBIC WALKING TRAINING		
Week #	**Phase**	**Duration (min/day)**	**Intensity (% max heart rate)**	**Frequency (days/wk)**
1-4	Progression	25	50	3
5-8	Progression	30	55	3
9-10	Progression	35	55	3
11-12	Progression	40	60	3
13-16	Progression	45	60	3
17-19	Progression	45	65	3
20-26	Progression	45	70	3
27-52	Maintenance	45	70	3

Appendix 3.2 Health Resource Utilization Questionnaire

HEALTH RESOURCE UTILIZATION QUESTIONNAIRE

This next set of questions asks about the **last 3 months**. We would like to know how often you saw health professionals, such as specialists, family physicians or allied health professionals, how often you had diagnostic tests and procedures performed and had blood tests taken, and how often you took medications. We also would like to know how often you were unable to do housework, whether you used community services due to illness and whether you missed a full day of paid work because of your illness.

Some health services are used very frequently, and others less frequently. You have different options to answer each question:

If the health service was received rarely you may choose this option:
_____ **times during past three (3) months**
If the health service was received more frequently, you may choose this option:
_____ **times per month**
If the health service was received very frequently, you may choose this option:
_____ **times per week**

1. How often did you make visits to your **family physician or a general practitioner**:
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not see a family physician/general practitioner

2. How often did you make visits to **physician specialists** either as an outpatient or in their office (for example: rheumatologist, endocrinologist, gynaecologist, orthopaedic surgeon,…)
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not see a specialist

3. How often did you make **visits to allied health professionals** (for example: physiotherapist, or other health professional, such as occupational therapist, kinesiologist, massage therapist, acupuncturist, nurse practitioner, chiropractor):
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not see any allied health professionals during the past 3 months

4. How often did you have **diagnostic tests or procedures** performed (for example: magnetic resonance imaging scan, computerized tomography scan, bone densitometry, x-rays, endoscopy, neurological tests, other diagnostic imaging test, .):
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not have any diagnostic tests or procedures during the past 3 months

5. How often did you have **blood withdrawn for laboratory tests:**:
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not have any blood withdrawn for laboratory tests.

Appendix 3.2 Health Resource Utilization Questionnaire (continued)

6. How often were you **admitted overnight to a hospital department** and the length of these visits (if you did not stay overnight, e.g. day surgery, please put 0 nights):
_____ times during past **three (3) months**
1st stay: _____ nights
2nd stay: _____ nights
3rd stay: _____ nights
☐ I did not make any visit to hospital departments

7. How often have you **visited a hospital emergency** department:
_____ times during past **three (3) months**
1st stay: _____ nights
2nd stay: _____ nights
3rd stay: _____ nights
☐ I did not make any visit to hospital departments

8. How many different **prescription drugs** are you taking at the moment:
_____ number of prescription drugs
☐ I don't take any prescription drugs

9. How many different **non-prescription drugs** are you taking at the moment: (for example: painkillers, vitamins, antacids, alternative therapies, herbal remedies, etc.):
_____ number of non-prescription drugs
☐ I don't take any non-prescription drugs

10. How often have you used any **community services** (for example: transportation, homecare, meals on wheels) during the past 3 months (answer for the one you have used most frequently)**:**:
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I did not use any community services.

11. How often were you unable to do your **normal daily activities**, e.g. housework, due to illness or injury during the past 3 months:
_____ times during past **three (3) months**
_____ times per **month**
_____ times per **week**
☐ I was able to do housework on all days of the past 3 months.

12. How often have you missed a full day of **paid work** due to illness or injury during the past 3 months:
_____ days during past **three (3) months**
_____ days per **month**
_____ days per **week**
☐ I did not miss a full day of paid work during the past 3 months.
☐ I am not engaged in paid work.

Appendix 4.1 Utility Values and Costs by Time Point (Pooled Results Using Multiple Imputation)

	Total N	Change from baseline utility ŧ		General Physician costs		Physician Specialist costs	
Walking							
Baseline	79	-	-	$75.80	($7.05)	$49.87	($8.38)
3 months	79	0.01	(0.08)	$62.88	($6.82)	$51.48	($7.19)
6 months	79	0.00	(0.08)	$78.01	($9.16)	$61.38	($8.34)
9 months	79	-0.01	(0.09)	$79.60	($5.32)	$77.88	($19.01)
12 months	79	0.00	(0.11)	$77.66	($6.87)	$64.77	($8.63)
15 months	79	0.00	(0.10)	$82.52	($7.86)	$78.59	($7.00)
18 months	79	0.00	(0.10)	$88.39	($7.46)	$74.27	($7.94)
Walking + Behavioural							
Baseline	69	-	-	$72.54	($5.66)	$74.38	($14.93)
3 months	69	-0.02	(0.09)	$69.27	($7.67)	$70.42	($11.18)
6 months	69	-0.01	(0.08)	$81.78	($8.39)	$78.36	($16.02)
9 months	69	-0.02	(0.09)	$76.04	($7.39)	$57.81	($12.60)
12 months	69	-0.02	(0.10)	$74.95	($7.87)	$66.16	($9.52)
15 months	69	-0.02	(0.10)	$88.00	($9.56)	$69.06	($12.47)
18 months	69	-0.04	(0.10)	$93.65	($8.64)	$81.45	($9.29)
Self-directed							
Baseline	74	-	-	$83.61	($11.67)	$54.32	($8.13)
3 months	74	0.01	(0.07)	$69.59	($7.08)	$55.01	($9.35)
6 months	74	0.01	(0.09)	$91.05	($11.79)	$61.67	($9.09)
9 months	74	0.00	(0.07)	$75.57	($7.95)	$70.46	($15.60)
12 months	74	0.01	(0.07)	$66.78	($6.14)	$70.33	($8.74)
15 months	74	0.00	(0.08)	$84.22	($8.69)	$65.75	($9.20)
18 months	74	0.01	(0.07)	$84.02	($9.46)	$71.01	($8.83)

Mean (SE) **Ł** Utility values calculated using last value carried forward

Appendix 4.1 (continued)

	Total N	Allied Health Professional costs		Diagnostic Test costs		Laboratory Test costs	
Walking							
Baseline	79	$193.16	($41.44)	$18.02	($2.65)	$8.69	($1.86)
3 months	79	$163.90	($31.77)	$16.46	($2.24)	$10.13	($1.89)
6 months	79	$149.41	($38.00)	$13.69	($2.02)	$11.78	($2.25)
9 months	79	$226.06	($43.44)	$21.86	($4.03)	$15.65	($2.64)
12 months	79	$517.22	($109.24)	$24.54	($3.12)	$14.89	($1.97)
15 months	79	$381.72	($69.48)	$28.05	($5.09)	$20.11	($2.95)
18 months	79	$329.92	($47.98)	$23.53	($4.02)	$19.49	($3.21)
Walking + Behavioural							
Baseline	69	$132.05	($32.85)	$17.12	($2.60)	$12.93	($2.12)
3 months	69	$91.60	($28.33)	$20.60	($3.97)	$14.85	($2.29)
6 months	69	$133.95	($26.98)	$14.18	($2.24)	$14.94	($2.12)
9 months	69	$202.89	($41.09)	$22.12	($4.00)	$16.17	($2.23)
12 months	69	$356.52	($70.05)	$22.36	($3.28)	$14.43	($1.71)
15 months	69	$262.21	($46.71)	$22.52	($3.70)	$19.46	($2.54)
18 months	69	$253.98	($49.40)	$17.15	($2.57)	$20.98	($2.55)
Self-directed							
Baseline	74	$247.68	($58.52)	$15.46	($3.16)	$10.84	($1.29)
3 months	74	$109.06	($22.63)	$13.67	($2.43)	$9.02	($1.31)
6 months	74	$185.22	($38.95)	$16.10	($2.80)	$16.48	($2.53)
9 months	74	$204.69	($38.01)	$22.22	($3.47)	$14.01	($2.06)
12 months	74	$424.38	($97.03)	$21.15	($3.31)	$12.73	($2.00)
15 months	74	$285.54	($61.52)	$19.93	($4.20)	$18.57	($2.39)
18 months	74	$254.03	($36.32)	$16.40	($2.62)	$20.45	($3.67)

Mean (SE)

Appendix 4.1 (continued)

	Total N	Overnight Admission Hospital costs		Hospital Emergency Department costs		Medication costs (daily)		Loss of productivity costs	
Walking									
Baseline	79	$26.47	($16.95)	$4.82	($2.10)	$1.78	($0.16)	$132.90	($46.00)
3 months	79	$50.24	($21.95)	$10.80	($3.19)	$1.79	($0.15)	$40.08	($24.37)
6 months	79	$91.81	($38.51)	$8.21	($2.17)	$1.84	($0.16)	$15.62	($9.63)
9 months	79	$54.85	($17.02)	$16.85	($5.48)	$1.87	($0.16)	$90.94	($36.36)
12 months	79	$204.95	($45.86)	$23.17	($4.44)	$2.01	($0.15)	$33.44	($23.99)
15 months	79	$222.20	($82.19)	$24.99	($4.44)	$1.93	($0.10)	$15.55	($7.89)
18 months	79	$104.65	($24.22)	$24.46	($5.85)	$2.00	($0.15)	$0.00	($0.00)
Walking + Behavioural									
Baseline	69	$26.56	($26.56)	$4.41	($2.16)	$1.91	($0.19)	$34.45	($25.94)
3 months	69	$52.49	($20.95)	$9.51	($3.33)	$1.99	($0.20)	$7.67	($7.67)
6 months	69	$55.28	($16.25)	$4.64	($1.88)	$1.97	($0.19)	$7.60	($5.63)
9 months	69	$29.75	($10.56)	$11.89	($2.90)	$2.02	($0.21)	$7.60	($5.63)
12 months	69	$96.79	($22.61)	$11.57	($2.57)	$2.04	($0.18)	$0.00	($0.00)
15 months	69	$119.47	($28.01)	$14.90	($4.78)	$1.85	($0.12)	$2.53	($2.53)
18 months	69	$81.70	($24.74)	$22.71	($5.65)	$2.04	($0.19)	$25.32	($25.32)
Self-directed									
Baseline	74	$37.14	($21.15)	$11.50	($4.14)	$1.78	($0.25)	$171.28	($50.61)
3 months	74	$80.48	($23.46)	$12.81	($2.91)	$1.71	($0.20)	$106.82	($40.98)
6 months	74	$133.06	($34.61)	$13.89	($4.11)	$1.90	($0.24)	$92.51	($37.06)
9 months	74	$39.51	($8.62)	$14.28	($3.74)	$1.96	($0.25)	$68.83	($32.05)
12 months	74	$154.14	($28.72)	$19.90	($3.80)	$1.96	($0.23)	$33.20	($16.48)
15 months	74	$217.17	($76.01)	$26.52	($5.67)	$1.74	($0.11)	$59.31	($32.62)
18 months	74	$109.29	($21.69)	$25.25	($6.80)	$1.91	($0.18)	$14.24	($12.08)

Mean (SE)

Appendix 4.2 Costs (Canadian $) and QALYs (Complete Data Only)

	Walking (n=39)		Walking + Behavioural (n=38)		Self-directed (n=30)		Walking vs. Self-directed (difference)	Walking Behavioural vs. Self-directed (difference)
Intervention costs	$417.02	-	$581.24	-	$34.85	-	$382.17	$546.39
General Physician costs	$415.53	($230.03)	$411.83	($298.11)	$301.83	($230.00)	$113.70	$110.01
Physician Specialist costs	$243.63	($202.14)	$285.42	($256.62)	$138.35	($117.11)	$105.28	$147.08
Allied Health Professional costs	$1223.93	($1,491.33)	$697.83	($1167.28)	$568.06	($813.56)	$655.87	$129.78
Diagnostic Test costs	$109.55	($92.42)	$82.95	($71.99)	$39.43	($48.69)	$70.13	$43.52
Laboratory Test costs	$76.38	($76.63)	$69.57	($66.27)	$43.95	($45.33)	$32.42	$25.61
Overnight Admission Hospital costs	$278.34	($662.81)	$46.03	($198.14)	$91.62	($279.55)	$186.72	$-45.59
Hospital Emergency Department costs	$56.37	($133.46)	$26.11	($59.65)	$15.00	($36.49)	$41.38	$11.11
Medication costs (daily)	$11.60	($6.55)	$11.03	($7.83)	$7.57	($5.95)	$4.02	$3.46
Loss of productivity costs	$239.06	($732.89)	$167.05	($972.37)	$940.29	($2,486.36)	$-701.22	$-773.23
Total Health care costs	$2,415.33	($2,277.05)	$1,630.77	($1,452.00)	$1,205.79	($1,182.74)	$1,209.54	$424.98
Total Societal Costs	$2,654.39	($2,617.18)	$1,797.82	($1,923.65)	$2,146.08	($2,734.62)	$508.31	$-348.26
QALYs (non-baseline adjusted)	1.01	(0.11)	1.04	(0.11)	1.08	(0.10)	-0.07	-0.04
QALYs (baseline adjusted)	1.04	(0.18)	1.02	(0.17)	1.09	(0.16)	-0.05	-0.07

Mean (SD)

Appendix 4.3 Costs (Canadian $) and QALYs (Excluding Drop Outs)

	Walking (n=44)		Walking + Behavioural (n=42)		Self-directed (n=36)		Walking vs. Self-directed (difference)	Walking Behavioural vs. Self-directed (difference)
Intervention costs	$ 417.02	-	$581.24	-	$34.85	-	$382.17	$ 546.39
General Physician costs	$418.75	($218.62)	$398.85	($287.62)	$305.37	($217.17)	$113.37	$93.48
Physician Specialist costs	$250.25	($194.01)	$273.71	($253.84)	$144.86	($146.10)	$105.39	$128.85
Allied Health Professional costs	$1,308.41	($1,702.47)	$652.02	($1120.45)	$511.82	($755.92)	$796.60	$140.20
Diagnostic Test costs	$103.55	($89.47)	$79.22	($71.20)	$46.80	($48.34)	$56.75	$32.42
Laboratory Test costs	$79.64	($75.64)	$71.68	($67.27)	$49.44	($49.01)	$30.20	$22.24
Overnight Admission Hospital costs	$288.35	($642.23)	$63.46	($231.82)	$178.14	($650.39)	$110.21	$-114.69
Hospital Emergency Department costs	$58.67	($132.00)	$25.43	($57.63)	$29.67	($69.42)	$29.00	$-4.24
Medication costs (daily)	$11.17	($6.63)	$10.52	($7.81)	$7.55	($5.91)	$3.62	$2.97
Loss of productivity costs	$211.90	($693.22)	$155.30	($924.74)	$866.66	($2,288.19)	$-654.77	$-711.36
Total Health care costs	$2,518.80	($2,444.84)	$1,574.89	($1,402.15)	$1,273.65	($1,246.31)	$1,245.15	$301.24
Total Societal Costs	$2,730.69	($2,722.02)	$1,730.19	($1,847.95)	$2,140.31	($2,562.74)	$590.38	$-410.12
QALYs (non-baseline adjusted)	1.01	(0.11)	1.04	(0.11)	1.07	(0.11)	-0.06	-0.02
QALYs (baseline adjusted)	1.02	(0.17)	1.02	(0.17)	1.09	(0.15)	-0.07	-0.07

Mean (SD)

Appendix 4.4 Costs (Canadian $) and QALYs (Excluding Imputations)

	Walking (n=79)		Walking + Behavioural (n=69)		Self-directed (n=74)		Walking vs. Self-directed (difference)	Walking Behavioural vs. Self-directed (difference)
Intervention costs	$417.02	-	$581.24	-	$34.85	-	$382.17	$546.39
General Physician costs	$275.84	($242.24)	$288.60	($276.21)	$222.20	($260.87)	$53.64	$66.40
Physician Specialist costs	$180.16	($218.89)	$210.64	($261.75)	$127.36	($185.58)	$52.80	$83.28
Allied Health Professional costs	$798.70	($1419.84)	$438.39	($927.11)	$346.50	($647.43)	$452.20	$91.90
Diagnostic Test costs	$67.09	($81.50)	$61.89	($73.08)	$36.09	($54.02)	$31.00	$25.81
Laboratory Test costs	$50.01	($70.91)	$51.95	($62.07)	$34.59	($49.91)	$15.42	$17.36
Overnight Admission Hospital costs	$207.34	($636.82)	$38.63	($182.69)	$148.57	($625.74)	$58.77	$-109.94
Hospital Emergency Department costs	$37.41	($103.14)	$16.58	($46.99)	$25.69	($62.47)	$11.72	$-9.11
Medication costs (daily)	$7.46	($6.96)	$7.71	($7.55)	$5.64	($6.55)	$1.82	$2.07
Loss of productivity costs	$222.83	($639.05)	$112.33	($734.77)	$645.34	($1,884.85)	$-422.51	$-533.01
Total Health care costs	$1,624.01	($2,171.17)	$1,114.40	($1,301.72)	$946.63	($1,310.45)	$677.38	$167.77
Total Societal Costs	$1,846.85	($2,418.17)	$1,226.73	($1,636.93)	$1,591.98	($2,413.88)	$254.87	$-365.24
QALYs (non-baseline adjusted)	1.00	(0.12)	1.03	(0.13)	1.05	(0.12)	-0.04	-0.02
QALYs (baseline adjusted)	1.01	(0.18)	1.01	(0.17)	1.05	(0.17)	-0.04	-0.04

Mean (SD)

Appendix 4.5 Multiple Regression Analysis- Mean QALY score at 12 months

Covariate	QALY	SE	p
(Constant)	.259	.039	.000
W	-.012	.009	.193
WB	-.014	.009	.128
Obese	-.004	.007	.553
College	.007	.008	.414
Participant's Gender	.006	.008	.432
Participant's Age	.000	.000	.455
How many years have you had arthritis?	-.001	.001	.033
TotalbaselineMETS	0.00	.000	.588
BaselineUtility	.662	.041	.000

Dependent Variable: Mean QALY at 12 months
Obese: $\geq$ 30kg/m^2;College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day

Appendix 4.6 Multiple Regression Analysis- Mean QALY score at 15 months

Covariate	QALY	SE	p
(Constant)	.351	.051	.000
W	-.015	.012	.207
WB	-.018	.012	.145
Obese	-.008	.010	.419
College	.010	.011	.368
Participant's Gender	.006	.011	.562
Participant's Age	-.001	.001	.292
How many years have you had arthritis?	-.001	.001	.076
TotalbaselineMETS	0.00	.000	.668
BaselineUtility	.805	.054	.000

Dependent Variable: Mean QALY at 15 months
Obese: $\geq$ 30kg/m^2;College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values

Appendix 4.7 Regression Analysis- Total Health Care Costs at 12 months

Covariate	Cost ($)	SE	p
(Constant)	3043.868	899.229	.001
W	592.426	300.134	.052
WB	373.698	306.216	.226
College	-36.511	259.007	.888
Obese	-54.975	223.318	.806
How many years have you had arthritis?	-4.816	15.980	.763
Participant's Gender	230.329	237.150	.331
Participant's Age	-18.671	12.780	.144
PatientBaselineCosts	.678	.219	.002
TotalbaselineMETS	-1.916	2.106	.364

Dependent Variable: Mean Health Care Cost at 12 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health care costs

Appendix 4.8 Regression Analysis- Total Health Care Costs at 15 months

Covariate	Cost ($)	SE	p
(Constant)	4036.137	1172.505	.001
W	730.176	408.912	.080
WB	276.014	396.176	.487
College	-104.360	341.242	.760
Obese	-29.323	292.784	.920
How many years have you had arthritis?	-3.546	20.698	.864
Participant's Gender	261.239	318.930	.413
Participant's Age	-23.841	17.170	.165
PatientBaselineCosts	.893	.291	.002
TotalbaselineMETS	-2.898	2.726	.288

Dependent Variable: Mean Health Care Cost at 15 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health care costs

Appendix 4.9 Multiple Regression Analysis- Total Societal Costs at 12 months

Covariate	Cost ($)	SE	p
(Constant)	3684.833	873.698	.000
W	471.197	286.380	.104
WB	229.568	289.883	.431
College	-6.437	248.294	.979
Obese	37.686	211.564	.859
How many years have you had arthritis?	2.613	15.238	.864
Participant's Gender	167.823	227.807	.461
Participant's Age	-28.355	12.471	.023
SocietalBaselineCosts	.735	.168	.000
TotalbaselineMETS	-3.761	2.021	.064

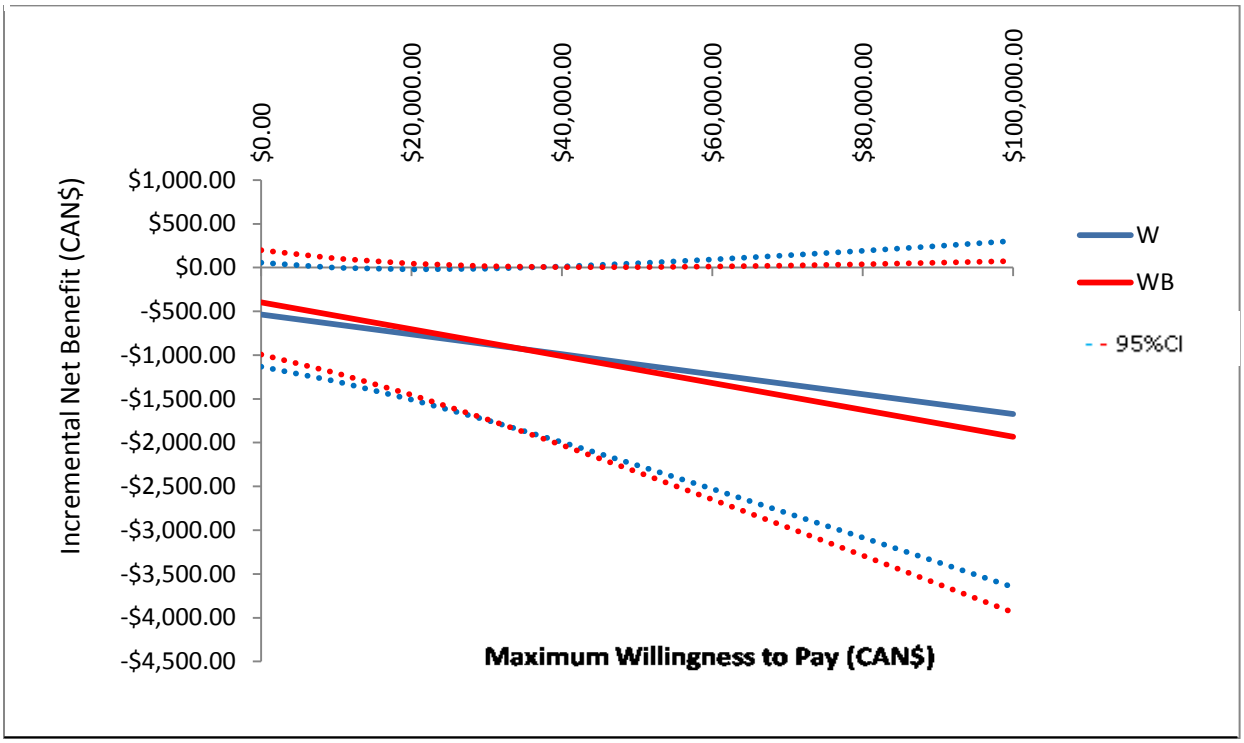
Dependent Variable: Mean Societal Cost at 12 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal costs

Appendix 4.10 Multiple Regression Analysis- Total Societal Costs at 15 months

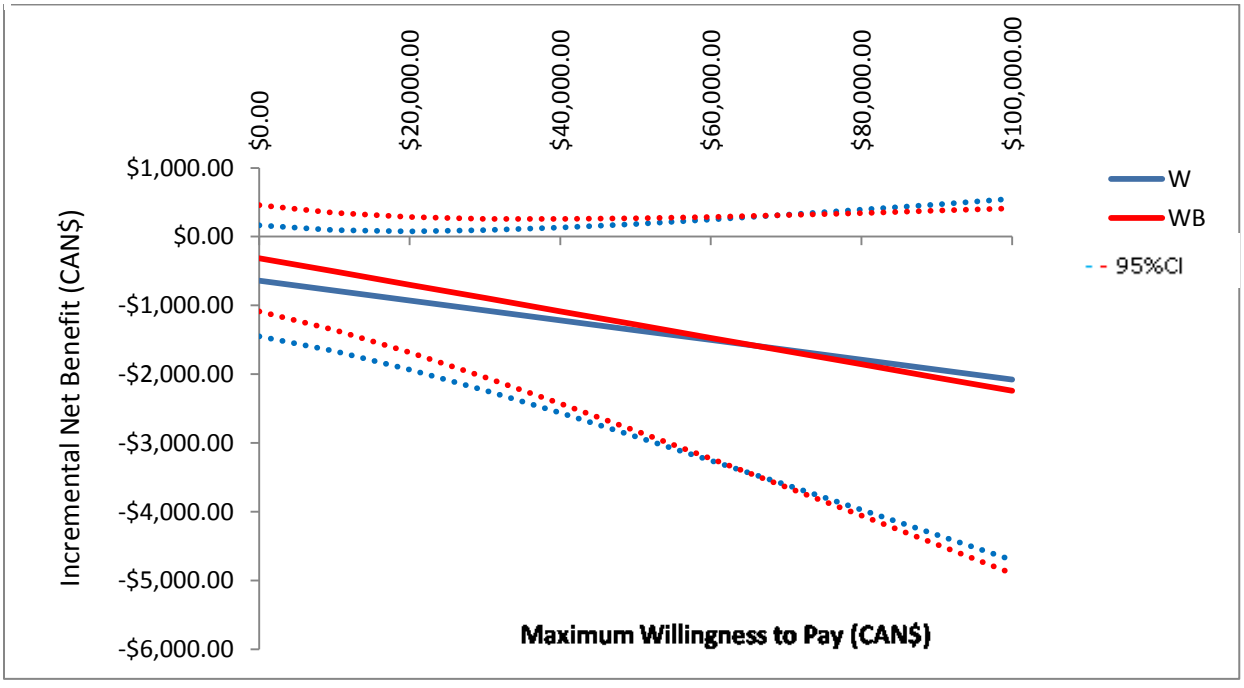
Covariate	Cost ($)	SE	p
(Constant)	4533.705	1131.353	.000
W	578.803	392.821	.147
WB	99.605	375.443	.791
College	-92.437	327.285	.778
Obese	74.599	277.600	.788
How many years have you had arthritis?	5.788	19.593	.768
Participant's Gender	254.038	307.507	.409
Participant's Age	-32.006	16.523	.053
SocietalBaselineCosts	.962	.214	.000
TotalbaselineMETS	-5.004	2.593	.054

Dependent Variable: Mean Societal Cost at 15 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal costs

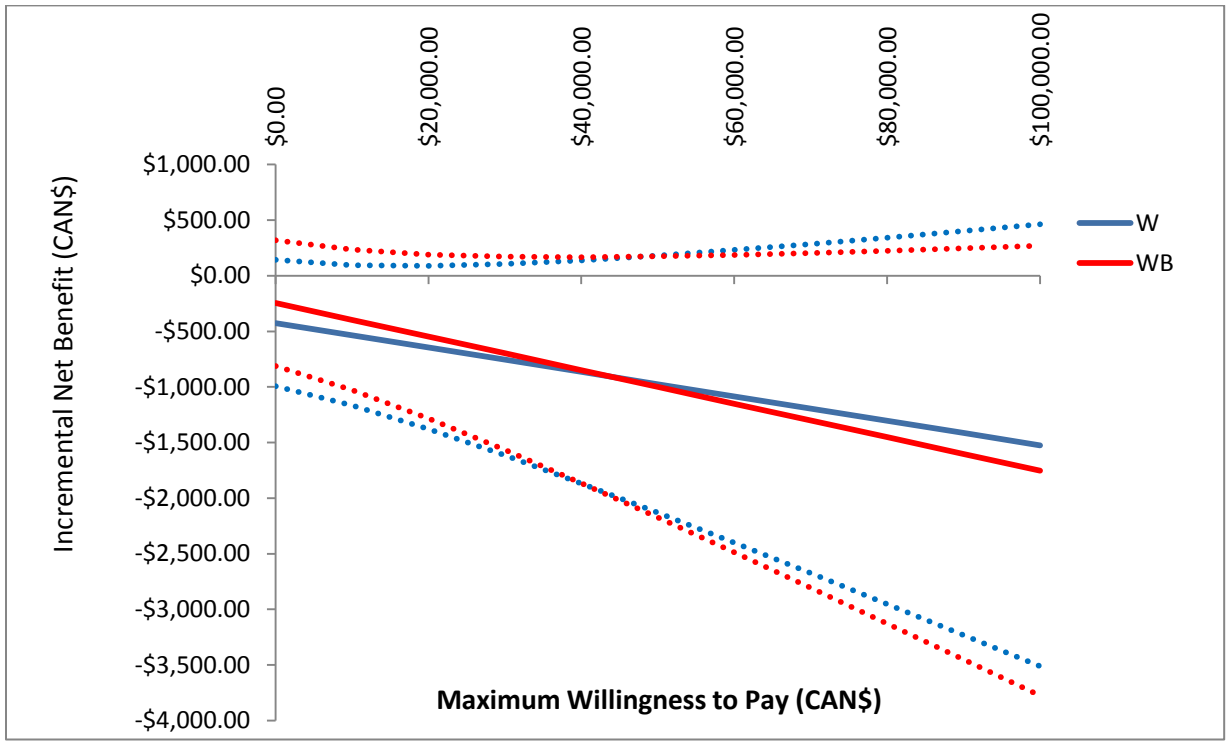
Appendix 4.11 Incremental Net Benefit of Walking Programs versus Self Directed Program - Health Care Costs at 12 months



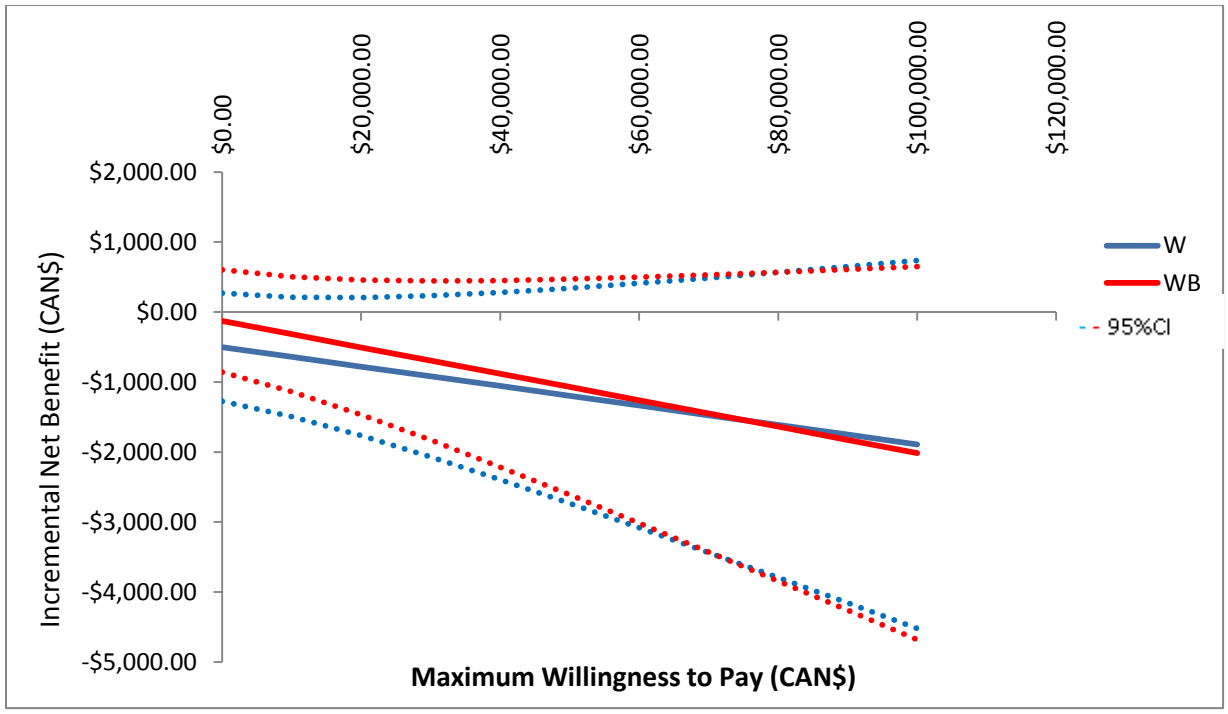
Appendix 4.12 Incremental Net Benefit of Walking Programs versus Self Directed Program - Health Care Costs at 15 months



Appendix 4.13 Incremental Net Benefit of Walking Programs versus Self Directed Program- Societal Costs at 12 months



Appendix 4.14 Incremental Net Benefit of Walking Programs versus Self Directed Program- Societal Costs at 15 months



Appendix 4.15 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Health Care Costs at 18 months

Covariate	INB ($)	SE	p
(Constant)	16184.966	4108.025	.000
W	-1515.134	926.982	.102
WB	-1640.934	934.233	.079
Participant's Age	-17.245	43.649	.693
Participant's Gender	-16.307	813.931	.984
How many years have you had arthritis?	-55.301	53.481	.301
Obese	-426.144	758.293	.574
College	768.145	844.642	.363
TotalbaselineMETS	.379	6.799	.956
PatientBaselineCosts	-1.069	.769	.164
BaselineUtility	49659.325	4281.074	.000

Dependent Variable: Incremental Net Benefit Health Care costs(WTP $50,000.00) at 18 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health Care costs

Appendix 4.16 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Societal Costs at 18 months

Covariate	INB ($)	SE	p
(Constant)	14797.517	4253.826	.001
W	-1378.223	941.211	.143
WB	-1402.759	952.563	.141
Participant's Age	-4.902	44.984	.913
Participant's Gender	-3.462	829.405	.997
How many years have you had arthritis?	-62.492	54.400	.251
Obese	-554.882	771.617	.472
College	715.208	866.204	.409
TotalbaselineMETS	2.307	6.950	.740
SocietalBaselineCosts	-.864	.607	.154
BaselineUtility	50109.376	4345.105	.000

Dependent Variable: Incremental Net Benefit Societal costs (WTP $50,000.00) at 18 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal costs

Appendix 4.17 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Health Care Costs at 12 months

Covariate	INB ($)	SE	p
(Constant)	9061.924	2606.579	.001
W	-1104.566	588.987	.061
WB	-1164.679	596.876	.051
Participant's Age	1.559	27.231	.954
Participant's Gender	36.134	508.532	.943
How many years have you had arthritis?	-41.742	33.751	.216
Obese	-83.971	474.282	.859
College	483.292	532.414	.364
TotalbaselineMETS	-.269	4.303	.950
PatientBaselineCosts	-.882	.481	.067
BaselineUtility	34439.641	2716.589	.000

Dependent Variable: Incremental Net Benefit Health Care costs(WTP $50,000.00) at 12 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health Care costs

Appendix 4.18 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Health Care Costs at 15 months

Covariate	INB ($)	SE	p
(Constant)	11929.855	3435.709	.001
W	-1359.123	788.055	.085
WB	-1278.108	788.281	.105
Participant's Age	-7.686	36.275	.832
Participant's Gender	-20.651	677.849	.976
How many years have you had arthritis?	-44.181	44.513	.321
Obese	-256.497	629.060	.683
College	727.025	706.164	.303
TotalbaselineMETS	.352	5.697	.951
PatientBaselineCosts	-1.073	.641	.094
BaselineUtility	42689.585	3573.222	.000

Dependent Variable: Incremental Net Benefit Health Care costs(WTP $50,000.00) at 15 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; PatientBaselineCosts: Baseline Health Care costs

Appendix 4.19 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Societal Costs at 12 months

Covariate	INB ($)	SE	p
(Constant)	8259.651	2664.261	.002
W	-974.987	589.996	.099
WB	-999.620	598.831	.095
Participant's Age	12.431	27.767	.654
Participant's Gender	114.597	512.444	.823
How many years have you had arthritis?	-48.469	33.910	.153
Obese	-187.271	476.440	.694
College	431.607	538.648	.423
TotalbaselineMETS	1.539	4.342	.723
SocietalBaselineCosts	-.722	.377	.055
BaselineUtility	34446.846	2722.672	.000

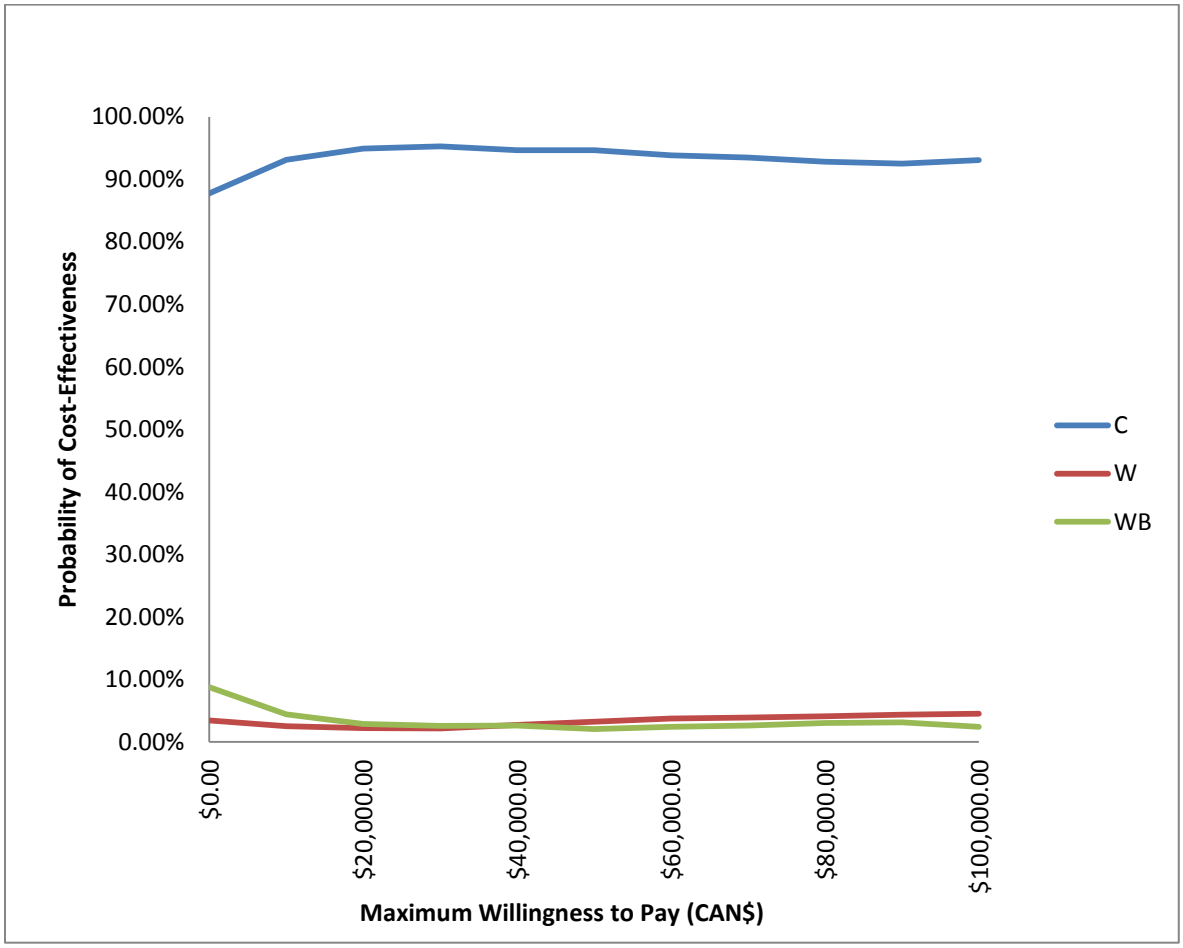
Dependent Variable: Incremental Net Benefit Societal costs (WTP $50,000.00) at 12 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal costs

Appendix 4.20 Multiple Regression Analysis- Incremental Net Benefit with a WTP threshold of $50,000.00 , Total Societal Costs at 15 months

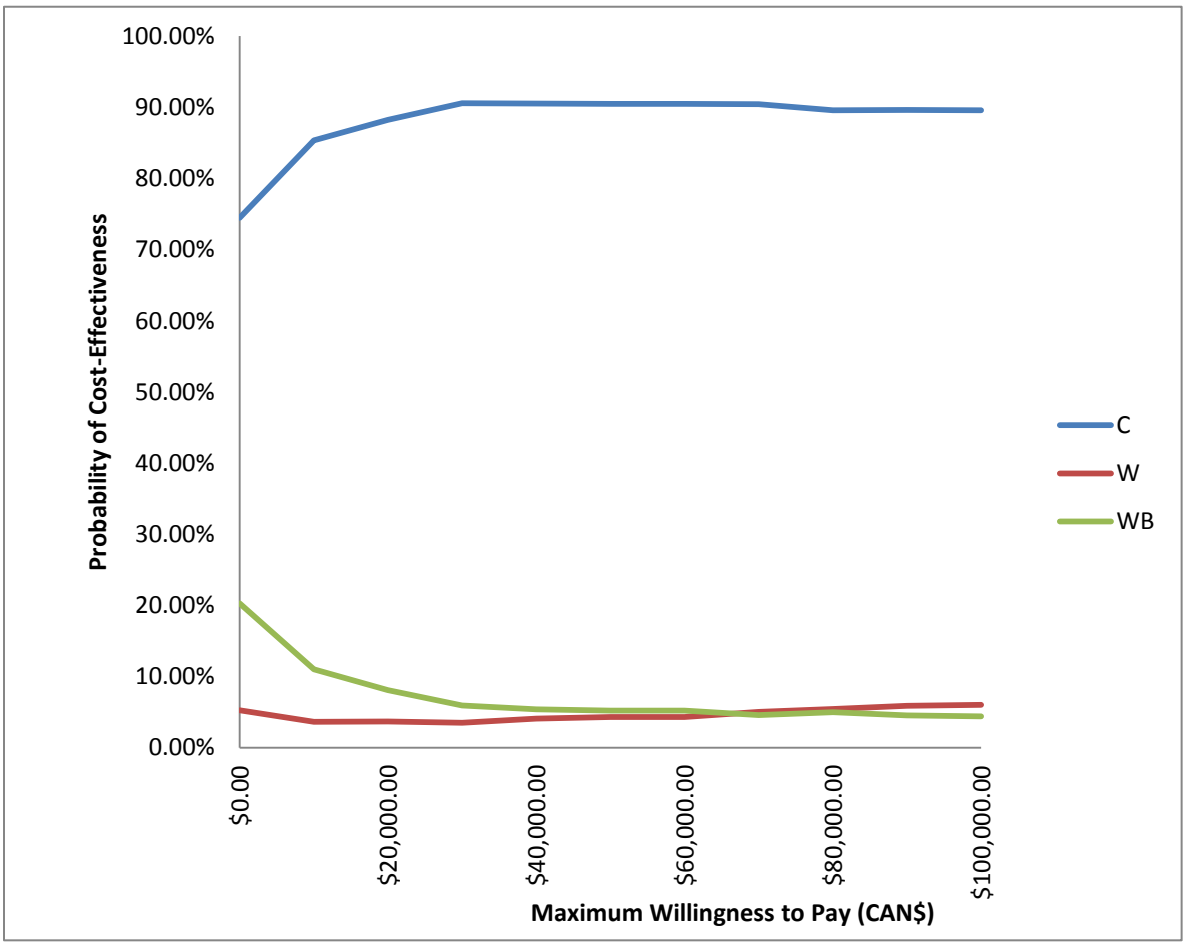
Covariate	INB ($)	SE	p
(Constant)	11144.461	3483.362	.001
W	-1196.556	784.211	.128
WB	-1071.051	785.984	.173
Participant's Age	2.511	36.610	.945
Participant's Gender	8.646	678.380	.990
How many years have you had arthritis?	-52.444	44.346	.237
Obese	-374.098	627.383	.551
College	680.054	709.550	.338
TotalbaselineMETS	2.345	5.702	.681
SocietalBaselineCosts	-.875	.494	.076
BaselineUtility	42774.672	3557.065	.000

Dependent Variable: Incremental Net Benefit Societal costs (WTP $50,000.00) at 15 months ($CAN)
Obese: $\geq$ 30kg/m^2; College: Education of some college or more; Age: Number in years; W: Walking Group; WB: Walking and Behavioural Group; TotalbaselineMETS: Baseline Intensity scores (7 day PAR); BaselineUtility: Baseline Utility values; SocietalBaselineCosts: Baseline Societal cost

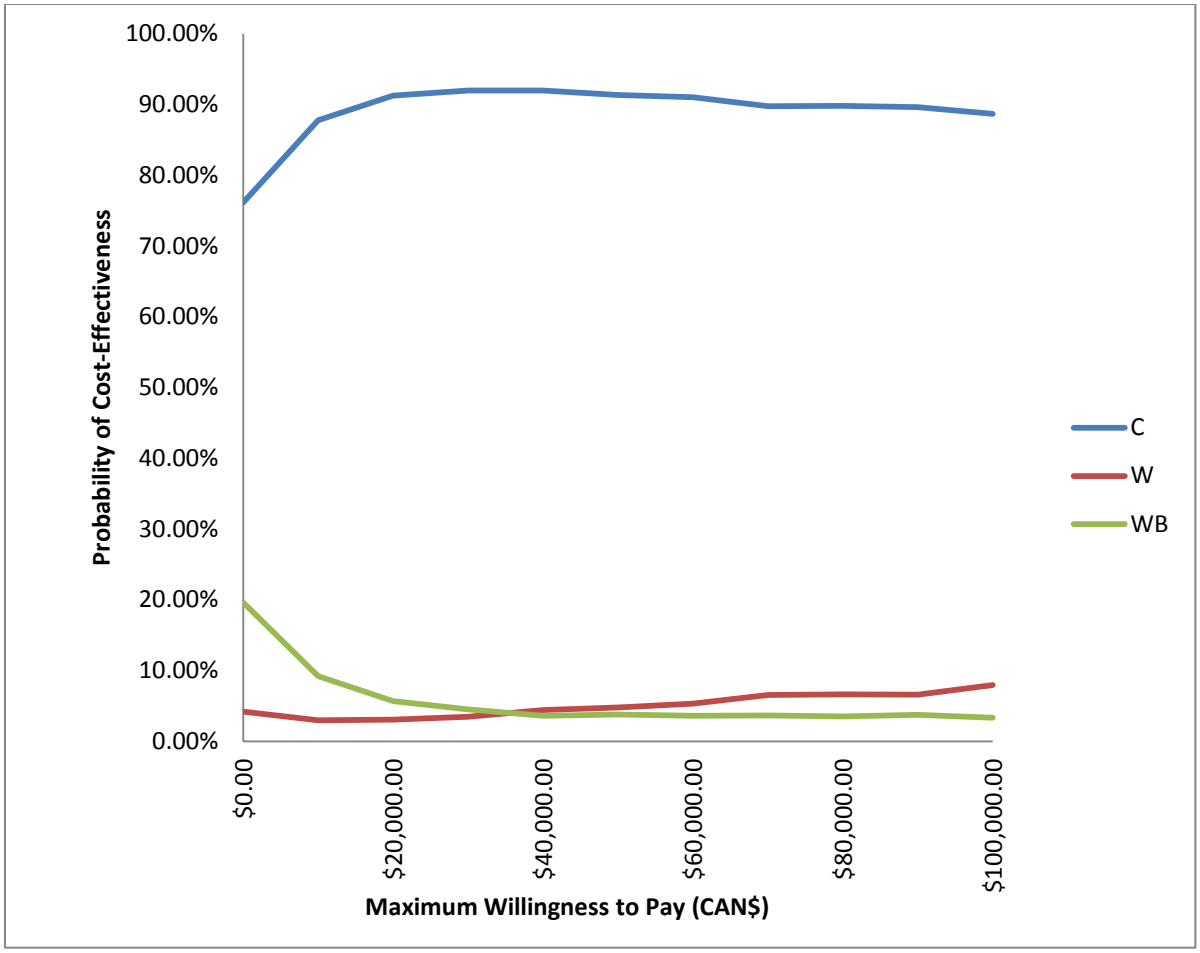
Appendix 4.21 Cost-Effectiveness Acceptability Curves Health Care Costs at 12 months



Appendix 4.22 Cost-Effectiveness Acceptability Curves Health Care Costs at 15 months



Appendix 4.23 Cost-Effectiveness Acceptability Curves Societal Costs at 12 months



Appendix 4.24 Cost-Effectiveness Acceptability Curves Societal Costs at 15 months