University of Alberta

Characteristics Associated with Increased Pain and Low Functional Recovery Three- Five Years Following Total Knee Arthroplasty

by

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Dedication

To my dad, Tim, for his endless encouragement

Abstract

The incidence of total knee arthroplasty (TKA) in Canada is steadily escalating; however, some recipients do not experience optimal outcomes.

The objective of this study was to identify patient demographics associated with inferior pain and functional outcomes at 3-5years post-TKA. A secondary objective was to identify changes in physical activity between pre-operative and 3-5 year post-TKA reports.

This was a secondary analysis of prospectively collected data of 743 TKA recipients. Univariate and multivariate analyses were performed for 3-5 year pain and functional outcomes on the Western Ontario McMaster Osteoarthritis Index (WOMAC).

Baseline variables significantly associated ($p < 0.05$) with 3-5 year WOMAC pain and function scores in the multivariate models were: age, BMI, back pain, WOMAC domain score, and SF-36 MH score. Daily activity and weekly walking levels tended to decrease after TKA.

Both pain and function models had low ability to predict outcomes, and sedentary activity increased post-TKA.

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List of Abbreviations

6MWT – 6 Minute Walk Test

ABJHI – Alberta Bone and Joint Health Institute

ACR – American College of Rheumatology

ADL – Activities of daily living

AKS – American Knee Society Score

AOS – Alberta Orthopaedic Society

BMI – Body Mass Index

CIRS – Cumulative Illness Rating Scale

DJD – Degenerative joint disease

HRQL – Health related quality of life

HSS – Hospital for Special Surgery Knee Rating

KOOS – Knee Injury and Osteoarthritis Outcome Score

KSS- Knee Society Score

LBP – Low Back Pain

LEFS – Lower Extremity Function Scale

LTFU – Loss to follow-up

MH – Mental health

NCP – New clinical pathway

OA – Osteoarthritis

PCL – Posterior cruciate ligament

PRO – Patient reported outcomes

SE- Standard error

SF-36 – Medical Outcomes Study Short Form

SOC – Standard of care

THA – Total hip arthroplasty

TJA – Total joint arthroplasty

TKA – Total knee arthroplasty

TUG – Timed Up and Go

VIF – Variance of inflation factor

WOMAC – Western Ontario and McMaster Universities Osteoarthritis Index

Chapter I

THE PROBLEM

Statement of the Problem

For aging individuals in Canada, degenerative joint disease (DJD) of the knee can be a significant source of pain and decreased physical function. As the most common form of DJD, osteoarthritis (OA) may significantly impact the health related quality of life (HRQL) of those diagnosed. While differing methods of management exist for mild to moderate knee OA, total knee arthroplasty (TKA) is the most common form of end stage disease management, with 94% of TKAs performed in Canada attributing OA as the primary precursor in 2006 – 2007. (1)

The prevalence of OA is estimated between 10-12% of the adult population in Canada, (2) with 27-37% having radiographic evidence, and 12-16% having symptomatic evidence in the population aged 65 and over. (3-5) A direct correlation between aging and disease incidence has been shown, with significant increases in prevalence occurring over age 65. (3) Gender variations also exist, with women having a higher prevalence of the disease across all ages in the population. (5) The correlation of age to disease has been demonstrated as less significant in men, (3) indicating that age and gender may interact with respect to disease presence.

Individuals with end stage OA experience advanced symptoms such as: debilitating pain, severe activity restrictions, long-term disability, depression, disturbed sleep, and increased contact with physician. (2) In these instances, patients may opt for an elective TKA. (6) The goal of arthroplasty among these patients is to relieve pain and restore function through the removal of the degenerated joint and insertion of a prosthetic implant. (7) The incidence of TKA performed in Canada has been steadily escalating, with a total of 47 249 knee replacements performed in 2008 – 2009, representing a 139% increase over the past 10 years. (1)

Joint arthroplasty has been shown to be a cost-effective and well utilized form of end stage disease management. (1, 8, 9) Patients receiving TKA typically experience alleviation of symptoms within the first 6 months following surgery. (10, 11) A smaller group of patients, however, experience little or no improvement in physical function and pain status post-operatively. It is estimated that this group represents 9% to 19% of TKA recipients. (12, 13) Currently, there is a lack of consensus regarding the factors that differentiate this poor outcomes group from those with greater improvements following surgery. (14-16) Determination of baseline characteristics and demographics associated with increased pain and negated functional improvement could assist in identifying patients who are less likely to benefit from the operation. Determining characteristics associated with lower levels of improvement would allow for better preparation of patient expectations and for possible adjustment of clinical treatment protocols to maximize outcomes.

The use of patient reported measures of pain and physical function as an outcome following surgery is a method that has become increasingly common.

(11) Patient reported outcomes have been described as more accurate assessments of health than physician described or clinical outcomes. (8, 17) For assessment of TKA, the Medical Outcomes Study Short Form (SF-36) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) are commonly used indices, (17, 18) and are typically completed pre and post-operatively. The WOMAC is a joint specific questionnaire assessing the domains of joint stiffness, pain, and function. While some research has been conducted to investigate predictive factors of pain and function scores on the WOMAC, little agreement has been reached.

Limitations of Current Evidence. There are several limitations of existing research investigating patient characteristics that predict poor outcomes. Primarily, many studies consist of a follow-up period of 6-12 months, leaving a gap in the evidence of patient characteristics associated with poor outcomes several years after joint replacement. Among the few studies which follow a cohort for a longer duration, sample size is often small (<100), thereby limiting the ability to detect important differences. Furthermore, given the limited amount of existing long term studies, it is difficult to reach a consensus regarding which factors are repeatedly predictive of poor long-term results following surgery. Variance exists among self-assessed outcome measures used by patients in longer term studies, prompting even less agreement about which patient factors are significant for one outcome (i.e. pain as measured by the WOMAC, SF-36, or Harris Hip Score).

A second constraint on the existing evidence is the use of physician reported measures as determinants of outcome. Measures such as strength, range of motion, and radiographic imaging have frequently been used to determine the success of a total joint arthroplasty (TJA). While such measures may be useful, they have not been consistently associated with patient reported outcomes post-operatively. (11, 14, 17) Given that patient measures are increasingly used as the indicator for surgical treatment, it is appropriate that similar measures also be used in defining outcomes.

A final limitation of previous investigations involves the method of statistical modeling used for determining predictive patient variables. Logistic regression has frequently been employed for statistical modeling of baseline characteristics to the outcomes of patient pain and function. The difficulty with this method is it dichotomizes patients into groups of high and low pain or function. In practice, this is not realistic as pain and function exist on a continuum rather than as discrete all-or-nothing groups. Individuals on the cusp of a cut-point for pain and function may be wrongly classified, creating study results that are misleading.

Based on previous evidence, it is clear that further research is necessary on predictive factors for poor outcomes following TKA. Specifically, there is a need for longitudinal cohort studies (> 2 years) with large sample sizes using the WOMAC as an outcome measure. More appropriate statistical modeling methods, such as multivariate linear regression, are also required.

Project Goals

The aim of this study was to identify baseline patient demographics associated with poor pain and physical function scores on the WOMAC. Modifiable and non-modifiable variables were investigated to determine the magnitude and direction of impact these factors have on patient outcomes. Results of this study may lead to several benefits for the patient. For identified characteristics which are modifiable, preoperative programs may be implemented to manage these traits. For those characteristics identified as non-modifiable, patient expectations may be set appropriately regarding the outcome of their surgery. Findings from this study will assist in preoperatively preparing the patient both physically and mentally to optimize outcomes post-TKA.

A secondary aim of this investigation was to determine any change between preoperative and postoperative physical activity levels. Activity levels were assessed using self-reports of activities performed at different intensities in hours per day, as well as using weekly walking levels as an indicator of overall activity. A description of change in activity levels from pre to post-TKA may guide clinicians when prescribing postoperative activity levels necessary for maintaining or improving health. Patients may be further educated on the amount of appropriate physical activities they ought to be performing following their joint replacement.

Expectations of the health professionals caring for patients with the identified variables may also be set accordingly. Resultantly, the health care professional's clinical treatment course may be modified to accommodate a patient's risk for poor outcomes.

Delimitations

The following study was delimited to subjects who:

1) were over the age of 29 who took part in the Alberta New Arthroplasty Model pilot project (19)
2) did not have a prior arthroplasty on the affected knee
3) did not have any terminal disease
4) were determined to have a life expectancy of greater than two years
5) did not have symptoms of dementia
6) had outcomes of pain and function as measured by the WOMAC in a self-administered manner

Limitations

The study data consisted of patients who received a TKA under either a newly developed clinical pathway, or who received the usual clinical care. As such, it is possible that observed outcomes were associated with a patient's allocation to one group or the other.

A limitation of the WOMAC as an outcome measure is the risk of floor or ceiling effects, meaning the index cannot detect low or high changes in score beyond the upper and lower boundaries on the predetermined measurement scale.

It is also possible that participants did not respond to the WOMAC with respect to their affected joint, as intended, but rather with respect to other ailments they may have been experiencing.

A final limitation of the study was the collection of follow-up data from a small number of subjects who did not respond to initial mail-out questionnaires through a telephone interview. It is possible that subjects answered questions differently when asked verbally by a research assistant, leading to the presence of interviewer bias.

Chapter II

LITERATURE REVIEW

Osteoarthritis

As defined by the American College of Rheumatology (ACR), OA is a "heterogeneous group of conditions that leads to joint symptoms and signs which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins." (20, p1039) Although this definition is widely accepted, it has been suggested that the ACR criteria reflect later stages of the disease, making OA assessment among the general population difficult. (21) OA is thought to occur as a result of several local and systemic factors, including: genetics, endocrine variances, muscle weakness and joint laxity. (3) It is proposed that a combination of these factors contribute to damage of the articular cartilage, particularly eroding and thinning of this tissue. (22, 23) Joint space narrowing ensues, leading to a bone on bone interaction during motion and ambulation. (24) It is these mechanisms which may be attributed to pain and stiffness in the older population. As the most common form of arthritis, OA has been cited as affecting 1 in 10 Canadians. (25) Typically this disease targets weight bearing joints such as the hip or knee, with degenerative OA being cited as the primary diagnosis for 81.9% of all THA and 95% of all TKA performed in Canada in 2009-2010. (26)

Traditionally, diagnostic criteria for OA have relied heavily on clinical evidence; however more recently diagnostic methods have emphasized two components: clinical and symptomatic evidence. (20) Clinical diagnosis relies primarily on radiographic evidence of structural change, usually indicating cartilage loss and joint space narrowing, as well as changes in the underlying bone. (27) Symptomatic osteoarthritis in the lower limbs is often defined in relation to pain experienced in the joint, limited mobility and functional loss. (28, 29) It is less frequent that radiographic evidence alone determines the course of OA management, as studies have indicated that less than half of those with clinical evidence are also symptomatic. (3) Resultantly, pain or limited physical function is often the determining criteria for surgical management. (2, 30)

Total Knee Arthroplasty

Treatment of mild to moderate OA frequently includes pharmacological treatments, rehabilitation therapy, and lifestyle and behaviour modifications. (6, 31, 32) In a systematic review assessing treatments of OA of the hip and knee, 51 treatment modalities from 23 existing guidelines were identified. Accepted methods of treatment include pharmacologic, non-pharmacologic, and surgical interventions, with TJA having a 100% agreement of effectiveness across guidelines. (33) Total knee replacement is indicated for patients when patients experience severe OA and do not respond to non-surgical treatments. In 2006 – 2007, the mean age of Canadians electing TKA was 68, with 61% being female and 39% being male. Trends toward a younger demographic as the recipient of this surgery have been observed, as the largest percentage increases in TKA were in the 45 – 54 year old age group for males (271%) and females (337%). (1)

It is forecasted by several researchers that the demand for TKAs will only increase in the coming years, as the size of the elderly population escalates (34, 35). The Public Health Agency of Canada projects that as a result of the growth of the aging population, one in every four people will hold status as a senior citizen by 2041. (36) The high prevalence of knee OA, the increases in existing rates of TKA, and the projected growth of the elderly population creates a climate for drastic increases in the number of necessary TKAs in the coming decades.

The TKA procedure involves removing the degenerated joint and replacing it with a prosthetic implant. Various surgical techniques and approaches are employed for TKA; however there is currently a lack of consensus regarding which methods are most optimal. Common surgical approaches include the medial parapatellar approach, the subvastus and midvastus approaches, and the lateral approach. (37) The medial parapatellar approach was once considered the standard in TKA, and involves incising along the medial border of the quadriceps tendon to allow for greatest exposure of the knee joint. In recent years, however, it has received criticism regarding subsequent patellar destabilization. The subvastus approach has been suggested as an alternative, where the joint is approached inferior to the vastus medialis. In cases where a subvastus approach was used, improvements have been noted in patellar tracking and knee flexion in the earlier stages of recovery. A consistent drawback reported with the subvastus approach is its limited joint exposure. For increased accessibility to the joint, a midvastus approach was developed which involves splitting the fibres of the vastus medialis. Finally, the lateral approach allows the knee joint to be accessed along the lateral border of the patellar tendon, and is most commonly indicated for TKA in valgus knees.

Variation among fixation techniques implemented during TKA also exists. Implants may be cemented, cementless, or hybrid systems. (38) Although indications for certain fixation techniques may vary, it has been reported that advantages for cementless TKA include shorter operative time and possible improved durability. In contrast, advantages for cemented techniques includes the creation of a seal which protects against debris caused by wear, as well as improved distribution of stress to the bone surrounding the prosthesis.

Additional TKA surgical factors to consider include patellar resurfacing, retaining or sacrificing the posterior cruciate ligament (PCL), and mobile versus fixed bearing surfaces. Indications for patellar resurfacing remain uncertain; however factors to consider include pre-TKA patellofemoral pain, patellar tracking, size, and quality of remaining articular cartilage. (39) The PCL may be retained or sacrificed during TKA, and current factors for this choice include the status of the PCL, surgeon preference, and the type of prosthesis being used. Although the current evidence is limited, it appears as though there is no difference between PCL retained and PCL sacrificed TKAs in terms of pain, range of motion, and stability. In instances where the PCL has been sacrificed, however, evidence indicates that prosthetics with a posterior stabilizing design are associated with improved range of motion. (40) Implants may also be mobile or fixed bearing, referring to the mobility of the polyethylene insert. The goal of the movable insert is to reduce stress across contact points of the joint and to improve range of motion. Current evidence comparing mobile and fixed bearing devices is limited, and no difference between devices has been observed. It has been hypothesized that differences in range of motion between bearing types may be due to an interaction with patellar resurfacing, however more evidence is required. (41)

TKA has been associated with improvements in knee joint pain among a large proportion of recipients. Patients receiving TKA can expect to experience some pain alleviation by 8 weeks to 6 months post-operatively. (42-44) Long-term pain improvements have also been shown for TKA, with some studies indicating improved pain relief at 3-5 years. (15, 45) While early pain improvements have been shown in TKA recipients, one investigation noted that mean pain scores remain worse than age matched population norms. (43) In some instances, pain improvements have been shown to regress slightly back to baseline levels following improvement. (45) It is uncertain whether this minimal decline is due to patient factors, or wear of the prosthesis.

Similarly, significant improvements in physical function have been shown among TKA recipients both in early and later stages. Functional improvements have been shown by 6 months (46) with some investigators reporting that the greatest early improvements in function occur in the first 6-9 weeks post-operatively. (47) Significant improvements in physical function have also been found over longer durations of 3-7 years. (48, 49)

Western Ontario and McMaster Universities Osteoarthritis Index

Patient reported outcomes (PRO) are often the preferred measurement tool for OA and TKA, given their simplicity, economic efficiency, and ability to be applied to a large scale. Valderas et al. (50) define PRO as “measurements of any aspect of a patient’s health status that come directly from the patient.” (p180) Self-assessments by patients are increasingly being used in conjunction with more traditional clinical measures. When used in clinical practice, it is suggested that patients benefit directly from these measures since their HRQL problems or deficits are directly identified for resolution. (51) These quality of life measures have been shown to be useful as screening tools, in monitoring changes due to an intervention, in facilitating communication between patient and clinician, and in prioritising treatments. (51) These measures can be the determining factor for a treatment course, since many treatments are costly or invasive and often not applied unless the patient perceives a certain threshold level of severity surrounding their condition.

The WOMAC is the most commonly used patient-based HRQL questionnaire in the assessment of: knee specific pain, stiffness, and functioning pre and post TKA. (52) Patient assessed HRQL is reported through 24 questions focusing on activities most relevant to the patient’s life. Of the 24 items in the questionnaire, there are: 5 pain, 2 stiffness, and 17 function items. A Likert scale is used to record the raw data, with a score of zero indicating the best outcome and 4 indicating the most extreme outcome. Overall WOMAC and subscale scores may be calculated by converting raw scores to a scale where zero represents the worst and 100 is the best outcome.

Reliability. Since its development several decades ago, the WOMAC has consistently been shown to be a reliable measurement tool for indicating the severity of arthritis and limitations of a joint. Wright and Young (53) assessed test-retest reliability of the WOMAC pre-operatively with 2 weeks between measurements. The duration of 2 weeks was chosen due to it being unlikely that clinical status would change drastically over this duration. Intraclass correlation coefficients described intra-rater reliability of the evaluations, where: pain ICC = 0.73, stiffness ICC = 0.53, and function ICC = 0.78. Inter-rater reliability of the WOMAC was also tested, yielding ICCs of: 0.80 for pain, 0.67 for stiffness, and 0.66 for function. These results are consistent with those found by Brazier et al. (54), who indicated no significant difference in WOMAC scores tested at a 2 week interval. A moderate level of reliability is assumed for ICCs of greater than 0.5, while a high level of reliability is assumed for ICCs greater than 0.70. Faucher and colleagues (55) conducted a similar test-retest protocol, using only a 3 hour interval between measurements of self-administered questionnaires. Reported ICCs for each domain were: 0.82 for pain, 0.68 for stiffness, and 0.74 for function. Investigators stated that an ICC of less than 0.65 would be considered insufficient evidence of reliability. Another study utilized the WOMAC as a validating tool for the EuroQol questionnaire, and both tools were self-administered 1 week apart in a test-retest protocol. Reliability for the WOMAC (using ICC) was: 0.65 and 0.80 respectively for pain and function domains (56).

Validity. Validity; or the ability of the WOMAC to measure the intended dimensions of pain, stiffness, and function; has also been repeatedly measured throughout the course of its use. An early study by Bellamy and colleagues (57) investigated the validity of the WOMAC in a population of OA patients receiving treatment with non-steroidal anti-inflammatory drugs. Internal consistency, a measure of how closely items measure a certain construct, was determined to have a Cronbach's alpha of 0.86 for the pain, 0.90 for stiffness, and 0.95 for physical function subscales. Bellamy et al. (57) also conducted a similar study among patients 6 weeks prior to total hip arthroplasty (THA), and found internal consistency to be 0.78, 0.75, and 0.92 respectively for the domains of pain, stiffness, and physical function. These results indicate that the WOMAC subscales are internally consistent, with each included item measuring a similar construct.

An investigation by Brazier et al. (54) described the validity of several measures of HRQL, including the WOMAC. Construct validity was tested by examining differences in scores between groups with mild/moderate and severe arthritis diagnosis using the Mann-Whitney U-test, with effect sizes of 0.95, 0.78 and 0.76 being reported for the pain, stiffness and physical function domains. Convergent validity was also established for the WOMACs physical function domain, as compared to the disability index of the Health Assessment Questionnaire (Spearman's rho = 0.68). Correlation at a level of 0.70 was also established between the pain dimension of the SF – 36 and the WOMAC. A separate study assessed discriminant validity of the WOMAC and SF – 36 in patients with and without knee disability and showed significant ability to detect differences between best and worst groups for each test. (58) Study authors cited, however, that the WOMAC had limited ability to discriminate disability due to causes not associated with the knee.

Responsiveness. Responsiveness of a measure refers to its ability to determine change when a change truly occurs. (59) Several studies have shown the WOMAC to be a responsive tool, as described by effect sizes which show a standardized measure of change between two groups. (60) As suggested by Cohen, (61) an effect size of 0.5 is moderate and 0.80 or greater is large. In an investigation by Thieler et al. (62), WOMAC responsiveness to the Lequesne-Algofunctional Index was compared, and effect size determined for patients at baseline and 6 months post-TKA. A global effect size of 2.25 was reported for the WOMAC, with the subscales of pain, stiffness and function having effect sizes of 2.40, 1.42, and 2.08 respectively.

Similarly, Brazier et al. (54) also found that pain was the most responsive subscale of the WOMAC in a study regarding various outcome measures of knee disability. Effect sizes of 0.95, 0.78, and 0.76 were reported for the domains of pain, stiffness, and physical function. These effect sizes are considerably smaller than the ones noted in the earlier study by Thieler et al.; (62) however one possible reason for the difference is the inclusion of subjects with mild to moderate OA severity along with TKA patients in the study by Brazier et al. Patients who do not have end stage OA may have less room for clinical change, resulting in smaller difference between measurements. A separate study of responsiveness in an OA cohort undergoing a 4 week rehabilitation program provided the similar result of pain being the most responsive subscale. Notably, this investigation also determined that the pain subscale was more responsive among female users. (63)

With respect to observable change between scores, another measure of interest is the minimally clinically important difference (MCID). This difference is defined as the smallest change in scores in a HRQL questionnaire that a subject perceives to be beneficial. (64) In a study analyzing the MCID in patients pre and post primary TKA, a WOMAC improvement of 19 points in physical function and 22 points in pain were necessary to be noted as an improvement by the patient. (65)

McConnell, Kolopack and Davis (59) indicate that the reliability of a measure affects the amount of true change that can be detected, as can smaller sample sizes. The reliability of the WOMAC can change between populations being studied; however given that it has been shown to be reliable among TKA patients, it is deemed to be a responsive measure for this population.

Other Considerations. Use of the WOMAC has grown to international proportions, with translated forms being validated across several languages. Adaptations of the WOMAC have been shown to be valid and reliable for use in various populations, including: French, Korean, Spanish, Swedish, Finnish, Turkish, and Thai versions. (55, 66-72)

One concern with the use of any Likert scaled HRQL questionnaire is the risk of floor and ceiling effects. Floor effects are said to occur when a high proportion of subjects place themselves in the lowest category for a HRQL item or domain. Similarly, ceiling effects are said to occur when a high proportion of subjects place themselves in the highest category of a HRQL domain. (65) In a previous investigation assessing floor and ceiling effects among TKA populations, it was determined that these effects were not significant preoperatively or at 6 months postoperatively, however a significant increase in ceiling effects were found at 2 years post-TKA. Floor effects remained constant across this time. (65) Study investigators stated that the WOMAC domains of pain and stiffness were most susceptible to these effects, given that they each contain fewer items to be measured. Other investigations have also found no significant impact of floor or ceiling effects pre-TKA, but significant ceiling effects at both 6 and 12 months were observed in the pain and stiffness domains. (69) It is necessary to watch for these effects in any study; however research indicates that a threshold of 15% is an acceptable amount for a study population to score at these levels. (73)

Predictor variables for poor TKA outcomes

Age. A limited number of studies exist assessing the predictive ability of age on scores of the pain or physical function subscales of the WOMAC. Bourne et al. (13) assessed the effect of age as a predictor in patient satisfaction of pain and physical function 1-year post primary TKA. Patient satisfaction was measured using a question of satisfaction, and providing three response categories: satisfied, neutral, and not satisfied. Age was shown to be a weak contributing variable to the prediction of low satisfaction in pain and physical function domains following surgery, with an odds ratio of 1.02 being reported for advancing age.

In a study by Escobar et al. (74), WOMAC scores were used as an outcome measure for predictors of HRQL improvements 6 months post-TKA.

Age was found to negatively correlate with pain and stiffness subscales on post-operative WOMAC measurements, but not with the physical function domain. A prospective study conducted by Jones et al. (75) compared the pain and physical function subscales of the WOMAC between older (>80 years) and younger cohorts (<80 years) at baseline and 6 months post-operatively. Study results showed no difference between groups, as well as no linear relationship of age to pain or physical function on the WOMAC subscales. Similarly, Kennedy et al. (47) found age not to be a significant predictor of any of the WOMAC subscales.

Fewer studies have been conducted assessing age as a predictor of pain or physical function over a longer post-operative duration, specifically when using the WOMAC as an outcome measure. One study found that increasing age was a significant predictor of poorer physical function scores on the WOMAC after a 3 year follow-up. In this investigation, lower WOMAC scores were designated as better outcomes, while higher scores indicated worse outcomes. A regression analysis found age to have a β coefficient of 0.37, indicating that for each 1 year increase in patient age, an increase of 0.37 will be observed in the physical function score. (48)

Other longitudinal studies using varying outcome measures include one by Nilsdotter, Toksvig-Larsen and Roos (76), which examined predictive factors of low pain and function outcomes as measure by the Knee Injury and Osteoarthritis Outcome Score (KOOS) over a 5 year follow-up. Increased pre-operative age was shown to correlate to elevated post-operative pain, but have no association with scores in the activities of daily living (ADL) domain at 5 years post-operatively. In contrast, a study by Elson and Brenkel (15) dichotomized patients into categories of good and poor pain outcomes 5-years post-operatively, as indicated by the American Knee Society score (AKS). Investigators found younger age to be a determinant of minimal or no improvement in pain following TKA, particularly when younger than 60. Study authors suggested that high outcome expectations and greater levels of physical activity aid in explaining modest surgical outcomes in the younger population. It has also been suggested that due to the prominence of comorbidity and other sources of pain, awareness of pain caused by TKA is lower among the elderly.

A separate study assessed age as a predictor of functional outcome 5 years after joint replacement, with poor function being defined as limitations in 2 or more specific ADL. Study authors found that subjects aged 71-80 and those older than 80 had odds of 2.4 and 4.7 of functional limitation as compared to subjects younger than 60. (77)

Several factors may be attributed to the conflicting findings of age as a predictive variable. Outcomes were not measured over the same time scale, nor were outcomes of pain and physical function attained with the same measurement tools. In fact, some outcome measures were generated for the purpose of the study, and have not been validated as thoroughly as others. (15, 77) Finally, several studies use age as a predictor of satisfaction in the domains of pain and physical function, while others directly assess pain and satisfaction from a joint specific measurement tool.

Gender. The predictive ability of gender on pain or physical function outcomes following TKA has been previously investigated, as has the effect of gender on morbidity and complications. Overall, female gender has been associated with greater length of hospital stay, as well as greater risk of complications within 30 days of surgery. (78) Numerous studies have also documented that women tend to have greater levels of pain and disability prior to surgery, (74, 78-80) with fewer studies showing no association. (81) It remains uncertain, however, whether gender is associated with differing levels of functionality and pain post-operatively.

Singh, Gabriel, and Lewallen (82) analyzed a large cohort of over 2600 patients 5 years post-arthroplasty for levels of pain using a question similar to the pain question used in the AKS questionnaire. It was found that at this time, women were not likely to experience different levels of moderate to severe pain than males, after adjusting for pre-operative pain and age. Following this investigation, Singh et al. (77) produced a study investigating whether limitations in physical function after knee replacement, as determined by limitation in 2 or more activities of daily living, was predicted by gender. Women were found to have greater moderate to severe limitations in physical function both 2 and 5 years post TKA, with reported odds ratios of 2.0 and 2.2 respectively relative to men. Over a shorter follow-up interval, Sharma et al. (81) found that gender was not significantly associated with the physical function domain of the SF-36 at 3 months after knee replacement; however the authors attributed non-significant findings to a small sample size.

Fewer studies exist using the WOMAC as an outcome measure when investigating gender as a predictive variable. One study using WOMAC subscales as outcomes at 6 months post-TKA found that gender was a significant predictor of all 3 WOMAC domains in a univariate analysis. However, once a multivariate analysis including the baseline WOMAC scores was conducted, gender was only predictive of the stiffness domain. (74) Similarly, Kennedy et al. (47) found that gender was a significant predictor of both pain as measured by the WOMAC pain subscale, and function as measured by the Lower Extremity Function Scale (LEFS), 1 week post-operatively. Gender, however, became non-significant for both domains once baseline pain and functional scores were considered. In a study with longer follow-up, Lingard et al. (79) also found that gender was not a predictive variable for WOMAC physical function scores at 1 and 2 years post-operatively. Conversely, Ghandi (48) found that female gender was a significant predictor of lower scores in the WOMAC physical function domain at 3 years, with females having an observed score of 4.55 points higher on this subscale.

Body mass index. The evidence surrounding the association between BMI and pain and functional outcomes following TKA is both limited and inconclusive. (83) Additionally, evidence is limited in that BMI is commonly assessed as a linear variable, rather than categorically as defined by the BMI classification system.

Sharma et al. (81) found no association between increased BMI and physical function as measured by the SF-36 at 3 months post-TKA ($p = 0.81$). A major limitation to this study, however, is that patients with a BMI > 51 were excluded from the analysis. This resulted in 17 patients being excluded, leaving 47 patients to participate in the study. Perhaps if inclusion criteria were not set surrounding maximum BMI, this variable would have approached significance. Ghandi et al. (48) also found that BMI did not significantly predict SF-36 physical function scores ($\beta = 0.06$, $p = 0.73$) or WOMAC function scores ($\beta = -0.06$, $p = 0.63$) in a multivariate analysis after accounting for other patient level predictors. The findings of this investigation are limited by the time of follow-up, as sample responses ranged from 1 – 8 years following TKA, and time of follow-up was determined to be a significant variable in predicting outcome. Similarly, in a separate investigation with follow-up period ranging 5-11 years, no difference was found between any BMI classes at baseline and post-TKA global WOMAC scores. Results also indicated that BMI was not discriminant for the level of improvement a patient may expect following TKA. (84) Stickles at al. (85) also found no association between BMI classification and change in global WOMAC scores at 1 year post-TKA. Obese patients were found to be significantly more likely to experience greater difficulty ascending stairs (OR = 1.2, CI: 1.1, 1.4) and descending stairs (OR = 1.2, CI: 1.1, 1.3) at this time.

In contrast, Nunez et al. (86) found using multivariate analysis that patients with a baseline BMI > 35 kg/m^2 (class I and II obesity) has significantly worse WOMAC function scores at 7 years post TKA than their less heavy counterparts ($\beta = 6.3$, $p = 0.035$). Patients with a BMI > 35 kg/m^2 were also found to have significantly worse WOMAC pain scores at this time ($\beta = 9.7$, P <

0.001). In this analysis, investigators classified an increase in the β coefficient as a worse outcome in WOMAC score. Winiarsky et al. (87) also found that morbidly obese patients (BMI > 40) had significantly worse functional outcomes at 5 years post-TKA, as measured by the Knee Society Score (KSS), than those with lower BMI. Investigators hypothesized that inferior outcome following TKA among morbidly obese individuals may be due to difficulty aligning the tibia peri-operatively due to excess fat which limits tibial exposure. Increased BMI was also found to be a significant predictor of WOMAC function scores among a large cohort of patients (n=1750) at 2-7 years post-TKA ($p = 0.02$). (49)

In a comparison between patients with painful and not-painful outcomes, patients who experienced greater pain at 1 year follow-up were more likely to have a higher BMI than those who experienced less pain (33.6 kg/m^2 compared with 30.5 kg/m^2, $p = 0.05$). (88) Investigators hypothesized increased pain was a result of greater forces on the joint, as well as increased soft tissue impingement. Jones et al. (89) also investigated the impact of obesity on pain and functional recovery following TKA. Severe obesity (defined as BMI ≥ 35) was significantly associated with better WOMAC pain scores at baseline ($p = 0.03$), as well as with better WOMAC function scores at 6 months ($p = 0.01$). No significant differences were found between BMI groups and WOMAC pain and functional outcomes at 3 years. Study authors attribute some of the heterogeneity among the existing evidence to difficulty defining obesity, particularly when considering age-related changes.

Comorbidities. Osteoarthritis is rarely the only disease afflicting patients receiving TKA. It remains uncertain, however, to what extent these comorbidities impact outcome following arthroplasty of the degenerated joint.

Cumulative. While there are specific comorbidities commonly seen among TKA recipients, it remains undecided as to whether the cumulative number of comorbidities a patient has or specific comorbidities increase their risk for poor outcome.

Escobar et al. (74) used the Charlson Comorbidity Index to determine comorbidity as a predictor, specifically in individuals with a summed score of ≥ 2. In a univariate analysis, pre-operative comorbidities were significantly associated with poorer outcomes in all three domains of the WOMAC. In a multivariate analysis including pre-operative questionnaire scores, comorbidities were significant in predicting outcomes in both the bodily pain and physical function domains of the SF-36, as well as in the pain and physical function domains of the WOMAC. In a similar analysis by Lingard et al. (79), it was found that 46% of a cohort of 701 subjects reported having greater than 2 comorbid conditions. Regression analysis by these authors found that the increased number of comorbidities was associated with poorer outcomes in WOMAC pain and physical function domains.

In contrast, one study used the Cumulative Illness Rating Scale (CIRS) as an outcome measure, and found comorbidities were not significant in a model predicting WOMAC pain and physical function scores following TKA. (90) Sharma et al. (81) also showed that comorbidity was not significantly associated with negative outcome following TKA when measured by the CIRS. It is noteworthy that in this study, comorbidity was approaching significance in a multiple regression analysis, with the CIRS score having a p-value=0.054. Similarly, Ghandi et al. (48) found quantity of comorbidities, as determined by CIRS, were not significant predictors of WOMAC physical function scores, but were significant in predicting outcomes in the physical function domain of the SF-36. This variance indicates that some comorbidity measures may be more sensitive to specific outcome tools, or that more validation and standardization is required for specific comorbidity measures.

Specific Conditions.

Back Pain. A limited number of studies have been conducted examining back pain as a predictor of pain or physical function outcomes following TJA. Among the studies found, low back pain (LBP) as opposed to generic back pain has been investigated. Previous research has documented LBP as a common comorbidity in patients receiving total knee replacement (91, 92). A study by Wolfe (92) hypothesized that LBP would affect preoperative WOMAC scores, due to its limitations placed on ADL. Wolfe found that patients with knee OA reporting LBP had significantly worse WOMAC pain and function scores than those without LBP pre-TKA. In a study following patients for 6 months post-TKA, absence of low back pain preoperatively was significantly associated with greater improvement in the WOMAC pain and physical function domains. (74) Conversely, Sullivan and colleagues (93) found no significant association between pre-operative reports of LBP and WOMAC pain scores 6 weeks post-operatively; however a significant difference in scores was observed for the WOMAC physical function domain. Currently, there is little agreement among the few existing studies analyzing predictive ability of LBP on post-operative WOMAC scores. At the time of this investigation, no studies were found analyzing the effect of pre-operative LBP on WOMAC scores in the pain and physical function subscales over a longer term (> 3 years).

Mental Health. Psychosocial factors such as depression and anxiety have also been suggested as predictors of pain and function post TKA, as it has been postulated that medical status variables alone cannot account entirely for TKA outcomes. (94) Currently, a limited number of studies are available that analyze the predictive abilities of mental health (MH) on pain or physical function post TKA, particularly for patient follow up durations of greater than 3 years. Among existing studies, there is also a high level of heterogeneity for the methods used to measure MH in patient populations.

Sharma et al. (81) found that in a multivariate analysis, psychosocial variables were responsible for 15% of the variance in functional outcomes as assessed by the SF-36. A later study by Brander and colleagues (95) found that depression and anxiety significantly predicted pain 1 year post-operatively in knee arthroplasty patients, with pain indicated by the Knee Society visual analogue scale and McGill Pain Questionnaire. Preoperatively, investigators used the Beck Depression Index and the State-Trait Anxiety Index to assess the psychological state of the subjects. Study results also indicated that TKA patients with the greatest depressive symptoms pre-TKA were likely to experience the greatest pain post-operatively, suggesting a graded response. A later longitudinal investigation by Brander et al. (96) found again that pre-operative depression significantly predicted worse KSS in the function domain. This investigation determined that anxiety was associated with worse pain levels at one year post TKA, but not at the 2 year end point. Similarly, Lingard et al. (79) found poor SF-36 MH scores to be the most significant predictor of pain as measured by the WOMAC subscale at 1 year.

In a study using WOMAC pain and physical function subscales as an outcome measure, the presence of depression as a determinant of patient outcomes 6 weeks post-operatively was assessed. The Patient Health Questionnaire-9 was used to assess pre-TKA depressive symptoms in study subjects. Pre-surgical depression was found to be significantly correlated with post-TKA pain and function in a univariate analysis; however in a multivariate regression analysis depression did not significantly predict post-operative pain or function. (93)

In contrast, Caracciolo and Giaquinto (97) found that absence of pre-operative depression was significantly associated with improved outcomes on the WOMAC pain and physical function subscales when depression was measured by the Hospital Anxiety and Depression scale. Improvements in scores remained even after adjusting for age and sex. Similarly, a study by Fisher et al. (88) determined in a logistic regression that patients who self-report depression pre-operatively have greater odds of experiencing stiffness and painful outcomes.

Study researchers hypothesized that depressive symptoms among those receiving joint replacement may hinder their desire to rehabilitate the joint post-operatively.

Recently, Merle-Vincent et al. (98) used the WOMAC as an outcome measure of pain and physical function, dichotomizing subjects into groups of satisfied and not satisfied following arthroplasty. Absence of depression pre-operatively was not significantly associated with improved TKA satisfaction 2 years post-operatively in a multivariate model; however absence of depression at the time of follow-up was predictive of greater satisfaction.

Diabetes. Previous investigations have noted that there is an increased incidence of diabetic patients receiving TKA in the past decade. (99) Diabetes has been previously shown to be associated with musculoskeletal abnormalities and limited joint mobility. (100) A positive diabetic status has also been shown to be associated with increased risk of post-TKA complications, such as deep infection and increased length of stay. (78) Given the limited amount of existing evidence, it remains uncertain whether a patient with diabetes at baseline will have worse pain or functional outcomes following TKA. To date, the effect of diabetes is often not tested individually, but is rather incorporated into a larger comorbidity cumulative score. Additionally, existing research has not used the WOMAC as an outcome measure of pain and function among diabetic patients.

Diabetes has been hypothesized to significantly impact post-operative pain levels, as it is a comorbidity which is commonly associated with increased bodily pain overall. (82) In a univariate analysis at 1 year post-TKA, Scott et al. (101) found diabetes not to be significantly associated with satisfaction for improvement in pain levels ($p = 0.29$). A separate study assessed joint flexion and pain at 1, 5, and 10 years post-TKA, and significantly worse results were found among diabetic patients when compared to age matched controls without the disease. (102) Fisher et al. (88) also found that after controlling for other patient demographics, baseline diabetic status was significantly associated with worse pain outcomes 1 year post-TKA.

Investigations with follow-up durations of > 2 years have demonstrated a lack of association between diabetes and inferior TKA function outcomes. Although diabetes appears to be a disease which affects overall mortality, its association to functional improvements is less apparent. In a follow-up of patients 2 years after their primary TKA, Singh (103) found that pre-operative diabetes was not significantly associated with worse function as measured by the SF-36 physical component summary score. In this investigation, diabetes was found not to be significantly associated with any domain score of the SF-36. The sample used for this investigation was comprised of veterans, and Singh notes that this population typically has greater levels of comorbidity than non-veterans. Given the higher prevalence of diabetes among this group, there was an increased likelihood of detecting significant differences if any existed. In a similar study with longer follow-up, Cushnaghan et al. (104) found that the presence of diabetes at baseline was not significantly associated with worse physical function scores on the SF-36 at 6 years post-TKA.

Lung Disease. The association between lung disease and inferior TKA outcomes has received less attention than associations with other variables, particularly because the direct effects of lung disease are often masked by its inclusion in a comorbidity summary score. Though lung disease has not been shown to be a predictor of patient satisfaction at 1 year post-TKA (101), its association to pain and functional outcomes is less certain.

At 1 year following primary TKA, pulmonary disease has shown significant associations to worse pain outcomes. When dichotomized into groups of painful or not painful outcomes, history of chronic obstructive pulmonary disease (COPD) was associated with worse outcomes ($p = 0.01$). (88) A secondary analysis of 165 primary TKA patients at 1 year post-operatively found a pulmonary diagnosis did not significantly predict WOMAC function in a multivariate model ($p = 0.063$). (105) While this investigation did not identify a significant association to functional status at this time, pulmonary diagnosis was approaching significance. Study investigators postulate that a larger sample size may have allowed for a significant detection.

At 2 years after their TKA, Singh (103) reported that in a population of veterans the presence of COPD or asthma was associated with statistically significantly worse SF-36 physical function scores ($p < 0.05$), but not bodily pain scores. Study investigators hypothesized that chronic lung disease impairs a patient's ability to fully participate in rehabilitation programs, thereby limiting their functional recovery.

Smoking status. Very little evidence was found regarding the effect of pre-operative smoking status on pain and function outcomes 3-5 years post-TKA. Most investigations on smoking status assess its effects on incidence and severity of osteoarthritis, or its association with post-operative morbidity, such as incidence of infection or other wound complications. (106)

One group of investigators found using a logistic regression analysis that positive smoking status pre-operatively was associated with better pain outcomes at 12 months post-operatively. While investigators cite that these findings are counterintuitive, one explanation offered is that the study may have been confounded by being conducted in a region with high smoking rates. (88) In regards to functional outcomes, Cushnaghan et al. (104) determined that status as a smoker or former smoker pre-TKA was significantly associated with worse SF-36 physical function scores at 6 years follow-up. Pre-operative healthy lifestyle education has been suggested as one means of reducing negative outcomes following TJA. (107)

At the time of this literature search, no other investigations were found assessing the predictive ability of preoperative smoking status on post-TKA pain and functional outcomes.

Social Support. To date, there is minimal evidence surrounding psycho-social variables and their association to TKA outcomes. The most common among these variables is the measure of social support, often reported as patient marital status. In these instances, social support can be considered as the availability of someone to care about the patient, and that the patient can rely on.

Escobar et al. (74) found that in a univariate analysis at 6 months following-TKA, patients who reported the presence of social support had greater improvements in WOMAC pain and function scores than those who reported no support. The association was also evident for both WOMAC pain ($p = 0.06$) and function ($p = 0.008$) outcomes at the multivariate level of analysis. Study authors suggest that improvements among those with daily social support are in part due to direct physical and material aids. In this investigation, authors suggest that presence of social support may be a factor to consider when deciding on surgical treatments.

Multivariate analyses also showed social support to be a significant predictor of both pain and function, as measured by the SF-36, at 1, 3, and 12 months post-TKA. Patients identified as either married or living with someone reported an average improvement of 9 points greater ($p = 0.004$) in the bodily pain domain and 6.3 ($p = 0.03$) points greater in the physical function domain across all three time periods compared to patients without support. (108)

No investigations assessing the impact that social support has on TKA outcomes beyond 12 months post-TKA. It is of interest to see the role this variable has in predicting long-term outcomes, as current evidence suggests that social support may only be critical in the early phases of post-operative recuperation.

Physical Activity. While there is a broad spectrum of levels of daily physical activity performed preoperatively by arthroplasty patients, the effects of this exercise on pain and functional outcomes are not well documented. Existing studies are limited to exercise as a part of a clinical plan for preoperative physical therapy plan to optimize functional status pre-TKA. Less emphasis has been placed on the natural amount of physical activity the patient engages in as part of their daily life.

A study by Williamson et al. (109) analyzed the impact of an exercise program implemented 6 weeks preoperatively on Oxford Knee Scores and overall WOMAC scores 12 weeks post-operatively. Patients completed 1 hour of quadriceps strengthening and stretching exercises, as well as functional exercises such as climbing stairs once a week for 6 weeks. Study findings were that no significant difference existed in overall WOMAC scores between the exercise group and the control group. A second study using the WOMAC as a TKA outcome measure also found no differences between exercise and control groups at 8 and 26 weeks post-operatively, even when exercise frequency was increased to 3 times a week for 6 weeks duration. (110)

Beaupre et al. (111) also investigated the effects of a preoperative exercise program and exercise education on pain, function, and HRQL. Patients were randomized into either a 4 week exercise group, or a patient education group. Patients in the exercise group attended the program at a physical therapy clinic 3 times a week and completed a standardized exercise program. Both groups were reassessed at 3, 6, and 12 months post-operatively using the WOMAC, SF-36, and several other measures of HRQL. No difference was found to exist between groups in any of the WOMAC subscales at any of the follow-up assessments. Additionally, no difference was seen between groups in the SF-36 subscales.

Rodgers and colleagues (112) assessed the impact of a pre-operative muscle strengthening program on TKA outcomes. A small sample size of ten subjects was used, with no significant differences being detected between treatment and control groups in range of motion, thigh circumference or 10 meter walk times. Pain and physical function were tested through the use of the Hospital for Special Surgery Knee Rating (HSS), and no significant differences were found to exist between groups. The HSS was also used in a study by D'Lima et al. (113) to investigate the effects of a preoperative strengthening program on TKA outcomes 6 weeks post-operatively as compared to a control group and a cardiovascular training group. Similar to the findings of Rogers et al., no significant differences in outcomes were reported between groups.

Preoperative Pain and Functional Levels. As identified by earlier research, pre-operative pain and function scores are often significant predictors of post TKA pain and function. A 2004 study by Long and colleagues (114) suggested that preoperative self-perceived health is often the greatest indicator of post-clinical intervention improvement in health status. The amount of literature examining the predictive capacity of these scores over longer durations and on large cohorts is limited.

An early study by Fortin et al. (90) investigated patient predictors of WOMAC pain and function subscale scores at 3 and 6 months post-operatively on a cohort of 92 TKA recipients. In a linear regression model, the best predictor of WOMAC pain scores at 6 months post-operatively was pre-operative WOMAC pain scores (β coefficient = 0.44), and the best predictor of WOMAC physical function scores at 6 months post-operatively was preoperative WOMAC physical function scores (β coefficient = 0.61). Patients with worse preoperative physical function were found to experience similar gains in pain and physical function scores post-operatively, but still had lower absolute pain and function scores compared to less severe preoperative groups. Fortin et al. interpreted these findings as an indication that earlier TKA treatment of OA would allow for more optimal outcomes, as disease management would occur before joint degeneration could progress to severe levels.

Predicted WOMAC physical function scores at 6 months post-TKA was also investigated by Jones, Voaklander, and Suarez-Almazor. (91) After adjusting for age and sex in a multiple linear regression model, preoperative WOMAC physical function scores was a significant predictor of post-TKA WOMAC physical function scores (β coefficient = 0.28). While the predictive results from Jones et al. are similar in direction to those from Fortin et al. (90), the magnitude of physical function as a predictive variable is dissimilar.

In an analysis of pain as a predictive variable on TKA outcomes in 116 subjects, Brander et al. (95) found that greater preoperative pain, determined by a visual analogue scale score of >40, predicted worse function 1 year post-operatively, as indicated by KSS. In a later study, Brander et al. (96) went on to investigate whether these results persisted long term, and analyzed 83 patients from the original cohort at 5 years follow-up. Study results showed nearly all subjects who reported elevated pain at 1 year follow-up were satisfied with their surgeries at the 5 year assessment, and experienced improved pain. Also, preoperative pain did not predict pain at 5 years, but did predict function at this time.

Using a smaller sample size of 152 subjects, Kennedy et al. (47) investigated variables significant in predicting post-TKA outcomes as measured by the pain and physical function subscales of the WOMAC, 6-minute walk test (6MWT), and Time Up and Go test (TUG). Study authors indicated that 6MWT and TUG test are appropriate measures of mobility and function in older arthroplasty patients. Preoperative scores for all 3 tests were found to be significant predictors of test scores 4 months post operatively.

A study by Nilsdotter et al. (76) also analyzed predictors of TKA outcomes on a small cohort of TKA patients (n = 102) at 6 months, 12 months, and 5 years post-operatively. The KOOS was used as an outcome measure, with study authors describing it as a valid and reliable extension of the WOMAC. The KOOS pain and ADL subscales were used, as improvement in ADL scores likely indicate improvements in physical function. With respect to pain, preoperative KOOS pain scores predicted equal improvements among patients of all severity at 12 months, however at 5 years follow-up patients with worse preoperative KOOS pain scores were found to have greatest decrements in KOOS scores. Similar results were found for the ADL subscale at 12 months and 5 years.

Cushnaghan et al. (104) later examined predictive variables of post TKA function as determined by the SF-36 using a case-control study design. Knee arthroplasty patients were matched with controls from the general population by age and gender, and follow up was completed in a range of 2-5 years. In the control group, better baseline physical function was associated with greater decline in physical function at follow-up, with controls experiencing a 3.7 point decrease in SF-36 physical function scores per 10 units at baseline. In the TKA group, higher baseline function was also associated with less improvement in physical function. For every 10 units reported in the SF-36 physical function score at baseline by TKA patients, an improvement of 4.7 fewer units at follow up could be expected.

Fewer studies exist with follow-up periods exceeding 1 year, or with sample sizes greater than 400. One cohort study followed 741 patients for 2 years duration, and analyzed the predictive ability of preoperative WOMAC pain and physical function subscales on post-TKA WOMAC scores. In this investigation, Lingard et al. (79) found using regression models that after controlling for age and gender, preoperative WOMAC pain scores were the greatest indicator of pain post knee replacement. This was found to be true for scores at both 1 and 2 years follow-up. Similarly, preoperative WOMAC function scores were found to be the most significant predictors of function at 1 and 2 years post-operatively. After dividing patients into quartiles based on preoperative WOMAC function scores, it was determined that TKA recipients in the lowest quartile (WOMAC function score < 34) experienced the greatest improvements in function scores; however they had quadruple the likelihood of reporting WOMAC function scores <60 at 2 years post TKA.

A separate study also used a large cohort of TKA recipients (n = 640), however observation took place over a shorter duration of 6 months. (74) Using the 3 WOMAC subscales as the dependent variable in a multivariate analysis, study results also indicated that preoperative subscale scores were the greatest predictors of postoperative WOMAC scores.

In a 3-year longitudinal follow-up on a cohort of 65 knees, Lavernia et al. (10) used the WOMAC and SF-36 as measures of function post-TKA to determine postoperative WOMAC scores. Subjects were dichotomized preoperatively into worse functioning (WOMAC function score >51) and high functioning (WOMAC function score ≤ 50) groups. Patients in the high functioning group were found to have better postoperative scores on the pain and physical function subscales of the WOMAC.

Clinical Relevance

The ability to predict outcomes at 3-5 years post-operatively based on preoperative characteristics may be quite beneficial to the patient. Depending on which associations between preoperative characteristics and post TKA outcomes are shown to be significant, patients may be better educated on what to expect several years following surgery. This process would allow for patient expectations to be set on a more individual level. As an example, older TKA recipients may be advised they might experience a certain degree of pain relief less than someone who is 10 years younger. If no differences exist between genders at 3-5 years follow-up, women may be told that although immediate improvements in physical function may appear slower than males, they can expect the same long term results. Individuals in poor health due to other causes may also be advised that as a result of their increased number of comorbidities, they might not achieve equivalent pain or physical function outcomes as a healthier person. Once these patients are aware of the risks for certain outcomes based on personal factors, they may more readily accept preoperative and postoperative rehabilitation and treatment plans to accommodate for their identified risks.

With respect to patient rehabilitation, significant findings from this study may also augment planned treatment courses. Clinicians may use study findings to better individualize rehabilitation programs based on patient risk factors. Preoperatively, interventions may be undertaken to remove or improve modifiable risk factors. If shown to be significant predictors of outcome, preoperative treatment strategies for low back pain may be implemented to alleviate this symptom before moving forward with surgery. Other clinicians may use similar methods for depression and anxiety. Results from this study may also assist clinicians in identifying which patients will require increased monitoring over a 3-5 year follow-up period, and who may have greater demands for long term treatments. Post-operatively, those at risk of poorer outcomes at 3-5 years might require participation in a rehabilitation program for longer duration than those without similar risks. Clinicians may identify these patients who will progress at a slower rate or to a lesser degree, and adjust physical demands and clinical expectations accordingly.

Chapter III

ARTHROPLASTY PILOT PROJECT

Study Goals

In 2003-2004, the Alberta Arthroplasty Study was conducted by Alberta Bone and Joint Health Institute (ABJHI), overseen by the Alberta Orthopaedic Society (AOS). In this investigation, conventional approaches to lower extremity joint arthroplasties were analyzed with the goal of developing an improved evidence based arthroplasty care model. The overall analysis of existing care determined that barriers to optimal arthroplasty care are: limitations and delays in physician referrals, poor patient screening and prioritization of referrals, delays in operative intervention due to insufficient surgical resources and hospital beds, and variability in preoperative and postoperative management. Based on these assessments, the AOS developed what they believed to be the ideal patient care model for hip or knee arthroplasty. A new clinical pathway (NCP) was developed by the Alberta Hip and Knee Replacement Project, and compared to the standard of care (SOC). A 2009 publication by Gooch et al. (19) assessed the development and implementation of this NCP model, and overviewed the effectiveness of clinical pathways.

The objectives of the Alberta Arthroplasty Study were to:

1. To compare patient outcomes including quality of life and adverse events
2. To compare activity based costs and efficiencies including acute care length of stay and operating room minutes
3. To compare cost-effectiveness

4. To assess patient satisfaction
5. To assess health care provider satisfaction

Design

A randomized control trial was used to compare the outcomes of the NCP with the SOC for THA and TKA. Data were collected prospectively, and eligible patients were consented, enrolled, and randomized. Participants were then followed for 12 months post-operatively. Further follow-up of these groups was undertaken in 2006 and 2009.

Twenty orthopaedic surgeons from the Edmonton, Calgary, and Red Deer regions who were identified as having high patient volume for lower extremity joint arthroplasties were responsible for referral of study subjects to ABJHI. Surgeons provided lists of patients to ABJHI for study enrolment based on their status as pre-surgical, a referral without a date for surgical consult, and new referrals. Eligible patients were mailed a package containing an information sheet, baseline questionnaire, and consent form. Patients were then randomized into either the NCP or SOC intervention groups.

Study analysis included both qualitative and quantitative methods. Descriptive statistics, multivariate models, and tests of effects were used quantitatively, while patient satisfaction surveys and interviews were used for qualitative data. An intention to treat analysis was used to assess outcomes. Aside from patient self-reported data, chart reviews of the NCP group were conducted to determine compliance with the program, patient wait times, and adverse events.

For patient follow-up at 3-5 years, data were collected by research assistants through the use of the same questionnaire at 3–5 years post-operatively. Questionnaires were mailed out to all participants, with each mail package containing an information sheet, a questionnaire, and a self-addressed stamped envelope for data return. For the 3–5 year follow up, a second mail-out was conducted within 6 months of the primary attempt to capture all participants who did not respond to the initial mail-out. Subjects who had not responded by the second mail-out attempt were then contacted by telephone, with two additional telephone calls made for subjects who were not reached on the first try.

Response rates were tracked by a research assistant through the use of an ACCESS database, and collected data were entered into a separate database. Patients were assigned a study identification number at the time of data entry.

Sample Size

Early sample size was determined as needing 1200 participants in the NCP group, as recommended by the Alberta provincial health ministry to ensure comprehensive evaluation of the program. The study was powered to 85% to detect changes from baseline to outcome in the SF-36 physical function domain, and to 99% to detect changes from baseline to outcome in the overall WOMAC score.

Participants

Participants for the study were chosen using a convenience sampling method. All patients were enrolled between April 1 2005 and May 4 2006, and received TJA before June 30 2006.

Inclusion criteria for the study were patients who:

1) were living in Alberta receiving a primary total hip or knee arthroplasty.
2) were at least 18 years of age

Exclusion criteria for the study were patients who:

1) had a total hip or knee arthroplasty surgery date booked within 3 months
2) were not referred for degenerative joint disease of the hip or knee
3) were not residents of Alberta
4) required joint resurfacing, partial joint replacement, or revision surgery
5) had a contraindication to participation in the study.

Intervention

The NCP is an all-encompassing evidence based care plan created to follow patients from the point of referral to 12 months post arthroplasty. The NCP is described as a multidisciplinary continuum of care aimed to improve quality and efficiency of treatment. Training of orthopaedic surgeons, clinic and hospital staff involved with the NCP was implemented, with all NCP health care workers being advised against providing any treatment services to those in the SOC group. While the list of changes in the NCP compared to the SOC is extensive, several key changes include: patient choice to refer to the next available surgeon, case manager assigned to each patient, patient education sessions and increased awareness of postoperative expectations, standardized health resource use pre-surgery, benchmark wait times for surgery, standardized surgical and subacute protocols, mobilization on day of surgery, and standardized health resource use post-operatively.

Outcomes

A total of 3434 patients were randomized in the study, with 1712 patients being assigned into the SOC group and 1722 into the NCP group. Of the patients randomized to the NCP group 1066 received surgery within the study time frame, while 504 of the patients randomized to the SOC group received surgery during the study time frame. Mean age of patients was 66 in both groups, and no mean baseline differences in WOMAC or SF-36 scores was observed between groups. In the NCP group, WOMAC scores improved 37.5 points from baseline to 12 months, and SF-36 scores improved 31.2 units in the physical function domain and 36.8 units in the bodily pain domain for the same duration. For the SOC group, WOMAC scores improved 34.5 points from baseline to 12 month measurements, and SF-36 scores improved 29.0 and 33.7 points for the respective physical function and bodily pain domains. At 12 months, the treatment effect of the NCP on WOMAC scores was 2.56, and 1.88 and 3.01 on the SF-36 physical function and bodily pain scores respectively. Treatment effects did not depend on joint replaced. Significant improvements were seen in all outcomes among the

NCP group, with the exception of SF-36 physical function scores which were shown not to be affected by the NCP among hip replacements.

Assessment

At 12 months, it was determined that the NCP significantly improved the HRQL among hip and knee replacement patients compared to the SOC group. Significant results were found in overall WOMAC and SF-36 bodily function scores for both joint replacements, and among knee replacements in the SF-36 physical function subscale. While it is was shown that significant improvements were found in the NCP group compared to the SOC group, it remains uncertain as to whether these differences are clinically significant. Study investigators stated that the effects of the NCP may have been underestimated, however, due to cross-over effect in the intention-to-treat analysis, and floor and ceiling effects of the WOMAC. Authors concluded that the NCP allows for greater improvements when compared to standard care.

Chapter IV

METHODS

Objectives

Primary Objectives. The primary aim of this study was to identify which patient demographic and baseline characteristics were significantly associated with high levels of pain or lower levels of function following TKA, as determined by the pain and function sub-scales of the WOMAC, 3-5 years post-operatively.

Baseline characteristics were determined through the use of linear modeling, and included: age, gender, BMI, marital status, comorbidities (cumulative and specific), preoperative pain levels as determined by the WOMAC, and preoperative physical function levels as determined by the WOMAC.

Secondary Objectives. A secondary objective for this study was to determine changes in physical activity from pre-surgical levels to levels reported 3-5 years post-operatively.

A descriptive analysis was performed on preoperative physical activity levels (not related to a clinical plan for rehabilitation or surgical preparation) and long term physical activity levels following TKA.

Hypotheses

Pain. With the WOMAC pain subscale as the outcome measure, and after controlling for other variables of interest, the research hypotheses for this study were that:

1) The effect of age on postoperative pain will be null, and no difference will be observed across age groups in pain levels 3-5 years following surgery
2) Gender will not be significantly associated with pain levels 3-5 years following surgery
3) BMI classifications greater than overweight will be associated with increased pain levels at 3-5 years post TKA
4) Subjects who are married or common law pre-TKA will have better pain scores at 3-5 years after surgery than those who are single, divorced, or separated
5) Those with increased numbers of comorbidities will have worse pain scores 3-5 years post-operatively
6) Pain scores at 3-5 years after surgery will be worse for participants who report presence of back pain at baseline
7) Subjects who are diabetic at baseline will have greater pain levels 3-5 years after surgery
8) Subjects with a pre-operative diagnosis of lung disease will not have worse pain scores 3-5 years post-operatively
9) Status as a smoker, or a history of smoking, will not be associated with pain levels at 3-5 years post-TKA
10) Worse SF-36 MH scores at baseline will be associated with worse pain outcomes 3-5 following surgery
11) Poor baseline WOMAC scores in the pain subscale will be associated with worse pain 3-5 years post-operatively.

Physical Function. With the WOMAC physical function subscale as the outcome measure, and after controlling for other variables of interest, the research hypotheses for this study were that:

1) Age will not be associated with function 3-5 years after surgery
2) Gender will not be associated with function 3-5 years after surgery
3) BMI will be predictive of function 3-5 years post-TKA
4) Participants who are married or common law pre-TKA will have better function scores 3-5 years after surgery than those who are single, divorced, or separated
5) A greater number of reported comorbidities preoperatively will be associated with worse function 3-5 years after surgery
6) Absence of back pain will be associated with improved function 3-5 years after surgery
7) Diabetic subjects will have worse function 3-5 years post-TKA
8) Diagnosis of lung disease at baseline will be associated with worse function 3-5 years after surgery
9) Status as a smoker, or smoking history, will not be associated with function 3-5 years post-TKA
10) Worse SF-36 MH scores will be associated with worse functional outcomes 3-5 years following surgery
11) Poor baseline WOMAC function scores will be associated with worse functional outcomes 3-5 years after surgery

Physical Activity. With quantity of physical activity as an outcome of interest, it was hypothesized:

1) that levels of physical activity will have increased 3-5 years post-TKA from observed pre-operative levels.

Operational Definitions

1) Osteoarthritis (OA) – A joint disease attributed to multiple factors which result in degradation of articular cartilage and underlying (subchondral) bone in the absence of inflammation.
2) Total Knee Arthroplasty (TKA) – A surgical procedure to replace the damaged knee joint, by replacing the tibial and femoral surfaces with metal or plastic prostheses. The patella being replaced when indicated.
3) Health Related Quality of Life (HRQL) – The value or condition of one's life as related to their impairments, disease, and psychological and functional states.
4) Pain – Physical discomfort caused by disease or injury.
5) Function – Physical ability to complete an action or task.
6) WOMAC – A 24 question health measure of pain, stiffness, and function specific to knee and hip osteoarthritis.
7) SF–36 – A 36 question multidimensional health measure of overall health state.
8) Statistical model – A mathematical equation describing how several independent variables are related to one dependent variable.

Study Design

This study was a secondary analysis of data from the Alberta Arthroplasty Study, a large longitudinal cohort study. Data for this cohort were collected prospectively. Only the subjects who underwent TKA surgery from the Edmonton and Calgary regions were included in the analysis.

Sample

For the purpose of this study, 743 patients receiving TKA from 17 surgeons in the Calgary and Edmonton regions were analyzed. Subjects were sourced from the Alberta Arthroplasty study, and were among the 1066 patients who were randomized and received surgery under the NCP group, or among the 504 patients from the SOC group. Subjects from these groups were excluded from this study if they were treated outside the Edmonton or Calgary regions, or if they received THA. Informed consent forms were signed by all participants at baseline and at the time of the 3-5 year mail-out, and an information sheet was provided discussing the study purpose, confidentiality, risks and benefits, and right to withdraw from the investigation (Appendix A).

Subjects who received a TKA from the Edmonton and Calgary regions were removed from the analysis if they were reported deceased at the time of follow-up, or if they no longer consented to be in the study at the time of the 3-5 year mail-out.

The sample size for the study was sufficient for determining predictive variables through a statistical model. One method of determining sample size for such multivariate linear regression models is:

$n \geq 10 * k$

where:

n = sample size,

k = number of independent variables to be analyzed. (115)

Thus, with this sample size, up to 74 variables can be included in the final model. For the purpose of this study, a total of 14 variables were considered during univariate analysis for inclusion in the final model. Based on the above equation, a sufficient sample size for this study is $n \geq 140$.

Study Setting

This secondary analysis examined patient data from the Calgary and Edmonton regions. At this time, participants were contacted by mail at their home addresses. Data analysis and management took place in the Orthopaedic Research office at the University of Alberta Hospital, with supplementary baseline information from the dataset in a secured repository at ABJHI.

Ethical Approval

Ethical approval for the primary study and long-term follow-up was granted from the University of Alberta and University of Calgary Ethics Review Boards. Approval was also received from the College of Physicians and Surgeons of Alberta Ethics Review Board. Further ethics approval was granted for secondary analysis of data from both University of Alberta and University of Calgary.

Dependent Variables

The primary outcomes for this study were the reported WOMAC scores in the pain subscale at 3–5 years post TKA, and in the physical function subscale at 3-5 years post TKA. A secondary outcome variable of interest was self-reported physical activity levels at 3-5 years following surgery. These variables were measured as continuous variables.

Independent Variables

Independent variables tested as continuous variables were: age, cumulative number of comorbidities, baseline WOMAC pain score, baseline WOMAC physical function score, baseline SF-36 MH score, and preoperative physical activity levels. Preoperative activity levels included the number of hours per day spent: sitting, performing slight, moderate, and heavy activity. Activity levels were also measured as categories of time spent per week walking for exercise or to work. Independent variables tested as categorical data included: gender, BMI, marital status, cumulative number of comorbidities, presence of back pain, diabetic status, presence of lung disease, smoking status.

Instruments

Several questionnaires were completed by subjects at the 3-5 year follow up point (Appendix B). Joint replacement history was recorded through a questionnaire indicating: joint replaced, side of replacement, and year of the surgery. A questionnaire aimed at collecting other health information was also completed, detailing: smoking history (never, past or current), quantity of cigarettes smoked, year started or quit smoking, and current alcohol consumption. A questionnaire in which 12 categories of disease were listed, with response options of: yes/no to presence of disease, year of onset, and specificity of type of disease was used to measure comorbidities. Binary responses of yes or no were used for the questions: currently receiving treatment, and any activity limitations due to disease. The SF-36 was used to obtain HRQL information, measuring 8 domains of general health. Depending on the domain, responses of yes/no or graded scores on a Likert scale were provided. The WOMAC was used to assess knee specific pain, stiffness and physical function. Responses ranging from "none" to "extreme" were recorded using a Likert scale. When more than one response was given for a question on the SF-36 or the WOMAC Likert scale, the more extreme or larger value indicated by the subject was selected and recorded as the final response for that question. A physical activity questionnaire was provided, tracking physical activity both qualitatively and quantitatively. Time spent performing 12 specific activities were recorded categorically, with response options ranging from "no time" to "> 11 hours per week." A separate table listed 5 categories of sedentary or physical activity behaviours and asked subjects to list the approximate number of hours per day spent performing each activity, to a summed total of 24 hours per day. A final blank table was provided for subjects to record any activities performed which were not previously listed in the questionnaire, frequency of these activities per week, and the duration of each activity.

Analysis

Raw WOMAC function scores were converted from a scale of 0 to 68, to a normalized scale of 0 to 100. Raw WOMAC pain scores were converted from a scale of 0 to 20, to a normalized scale of 0 to 100. Zero represented the worst outcome, and 100 indicated the best. Transformation of these scores were completed using a predetermined conversion code performed with the statistical software SPSS. Subjects missing greater than five points of data in the WOMAC were excluded from the analysis. Subject-specific imputations were used for participants who had five or less missing responses in the overall questionnaire, by assigning the missing question the mean score of all other responses in that subscale. The remainder of the data analysis was performed using the statistical software STATA. Threats to statistical conclusion validity were avoided through the use of a large sample size, and use of the WOMAC which has shown to be a valid and reliable outcome measures.

Descriptive Analysis. A descriptive data analysis was carried out on the baseline patient variables. Frequencies of gender and age were determined. Means and standard deviations were reported for baseline WOMAC pain scores and baseline WOMAC function scores. Means and standard deviations were reported for the continuous independent variables: age, BMI, number of comorbidities, and SF-36 MH scores. Proportions and frequencies were be reported for the categorical independent variables: years after surgery, group assignment, BMI, marital status, cumulative number of comorbidities, presence of back pain, presence of lung disease, presence of diabetes, smoking status. These values were reported both overall, and separated by gender. To assess for differences at baseline between genders, either a two sample unpaired t-test or a chi square test was used. The level of significance to detect differences was set at a p-value < 0.05.

The amount of change observed between baseline and 3-5 years was also reported for the variables: WOMAC pain scores, WOMAC function scores, SF-36 MH scores, and for the frequencies of cumulative and all specific comorbidities. Either a two sample paired t-test or a chi square test was used to determine significant differences between the two time points. The level of significance for the change in these variables was set at a p-value < 0.05.

Analysis of Losses to Follow-up. Frequency of responders at 3-5 years from the eligible baseline cohort was determined to indicate the proportion of subjects who did not provide follow-up data. This included counts of those who were unable to be contacted after several attempts, and those who relocated and provided no alternate means of contact. A descriptive data analysis of these individuals who were lost to follow-up (LTFU) was conducted. Baseline data for these subjects was analyzed to determine whether these individuals differed from the rest of the study sample. Means, standard deviations were reported for the continuous independent variables: age, BMI, number of comorbidities, and SF-36 MH scores. Proportions and frequencies were reported for the categorical independent variables: years after surgery, group assignment, BMI, marital status, cumulative number of comorbidities, presence of back pain, presence of lung disease, presence of diabetes, smoking status. Either a two sample unpaired t-test or a chi square test was used to compare each of these variables between the LTFU and the rest of the cohort. A p-value of > 0.05 indicated no significant difference between the two groups.

Univariate Analysis. A univariate linear regression was performed for the independent variables: age, gender, marital status, BMI (both linear and categorical), number of comorbidities (categories of ≤ 2 or ≥ 3 conditions), years after surgery, group assignment, presence of back pain, presence of diabetes, presence of lung disease, smoking status, baseline WOMAC physical function scores, baseline WOMAC pain scores, and baseline SF-36 MH scores. A partial F-test was used to determine the significance of each variable, and variables with a p-value < 0.05 were deemed significant predictors of the outcome of interest when considered individually. Each variable was tested twice; once for the outcome measure of pain, and once for the outcome measure of physical function. Coefficients for the continuous variables: age, BMI (linear), baseline WOMAC physical function score, baseline WOMAC pain score, and baseline SF-36 MH scores were interpreted as the amount of increase expected in outcome score per 1 unit increase in the independent variable. For the categorical independent variables: gender, marital status, BMI (categorical), group assignment, years after surgery, presence of back pain, presence of diabetes, presence of lung disease, smoking status, and cumulative comorbidities, coefficients were interpreted as the unit increase in outcome expected in the presence of that variable (compared to the defined reference group).

It was of interest to see not only which variables were predictive of pain or function on a univariable level, but which were non-significant when in the presence of other demographic variables. For the study's purpose of statistical modeling, independent variables shown to be significant at a level of $p < 0.20$ were carried over to the next step of multiple linear regression.

Multivariate Analysis. A multivariate regression analysis was performed to create a model fitted with independent variables that function as predictors of WOMAC scores following TKA. This analysis was performed twice; once with postoperative WOMAC pain scores as the outcome measure, and again with postoperative WOMAC physical function scores as the endpoint. A coefficient for each parameter was calculated to determine the magnitude per unit increase of that parameter on WOMAC scores. To determine the variables to be included in the model, a purposeful selection procedure was used. The variable group assignment was force entered into the models to control for any potential differences existing between the two treatment groups from the Alberta Arthroplasty Study. Independent variables shown to be significant at $p < 0.20$ in the previous simple regression were tested in the multiple linear regression. When tested in the multivariate model, significant variables from the previous simple regression which did not hold significance at the level $p < 0.05$ were removed. The significance of these variables was determined using a partial F-test. All significant variables remained in the statistical model as predictors of WOMAC scores. β coefficients, standard error (SE), and p-values for these significant variables was reported.

A test for confounding was performed on all variables excluded from the model, and any variable shown to alter a remaining coefficient by more than 15% was considered for re-entry into the model. Interactions between variables were tested using partial F-tests with full and reduced models, and interaction terms significant at a level of $p < 0.05$ were included. Interactions of interest included: age and gender, baseline WOMAC physical function score and BMI, baseline WOMAC pain score and BMI, gender and baseline WOMAC pain score, gender and baseline WOMAC function score, age and baseline WOMAC pain score, age and baseline WOMAC function score, cumulative comorbidities and SF-36 MH score, and baseline WOMAC pain score and SF-36 MH score. No test for outlier observations was conducted, as the WOMAC has potential for floor and ceiling effect on patient scores. As such, it is likely that a number of subjects reported extreme high and low scores.

Testing the Model

Several tests were conducted post analysis to confirm stability of the multivariate model. To determine the stability, both forward and backward stepwise regressions were performed, and significant variables from both models were compared to those found in the original purposeful selection model.

Forward Stepwise Selection. In the forward stepwise selection procedure, a simple linear regression was carried out for the dependent variable (either WOMAC pain or physical function scores) for all independent variables. Only variables with a significance of $p < 0.10$ were considered for entry into the model. Single significant variables from the univariate analyses were then added to the model, and checked to see if significance was retained ($p < 0.05$) once in the model. Variables that were previously entered were also checked to see if they remained significant in the presence of the newly added variable. Removal of previously entered variables occurred if their significance weakened at this point. The process of adding variables stopped when the variable with the highest significant p-value in univariate analysis ($p<0.10$) was no longer significant in the multivariate model ($p<0.05$).

Backward Stepwise Selection. In the backward stepwise selection procedure, a regression equation was fitted with all independent variables. Each variable was analyzed as if it were the last variable to enter the model (type III sum of squares) by determining a partial F-statistic and p-value for each. If the variable presented a p-value > 0.05, it was deemed non-significant and dropped from the overall model. If several variables were non-significant at this level, then the variable with the greatest p-value was dropped first, and the rest remained in the model. The regression was then run again to determine if the significance of any variables changed in the absence of the dropped variable. This procedure was repeated until all variables were significant. Variables in this final model were then compared to those remaining in the forward stepwise selection model, and the original purposeful selection model. Coefficients for each variable were also compared. Agreement among the three models with respect to included variables and the magnitude of their coefficients were used to indicate stability of the original purposeful selection model.

Collinearity. Following the multivariate regression analysis, a test of collinearity of the independent variables was performed. Correlation between independent variables was first determined using a pair-wise correlation test. Observed correlations assisted in determining which variables were necessary for removal following the collinearity test. To determine collinearity between two measures, variance of inflation factor (VIF) was calculated for each variable. A VIF > 10 was set as an indicator of collinearity. If a variable was shown to have a high correlation and a VIF > 10, it was removed and the collinearity test was run again. This continued until each variable had an observed VIF < 10.

Model Variance. The amount of variance, or how well the regression model fit the data, was tested using the coefficient of determination (R^2). Following the purposeful selection regression, the R^2 for the final model was determined for all included variables. This value was transformed to a percentage to indicate the extent to which the included variables were able to predict the specified outcome, and the remaining percentage of variance that was caused by other factors or error. Two R^2 values were reported; one for the physical function model, and one for the pain model.

Chapter V

RESULTS

Demographics

Respondents. Between April 1 2005 and May 4 2006, a total of 4985 subjects from the Edmonton, Calgary, and Red Deer regions were eligible to participate in the Alberta Arthroplasty Study. Among these subjects, 1551 refused to participate in the study while 3434 consented and were randomized to a treatment group. Among the included patients, 2090 were booked for a TKA. For the present investigation, 743 participants from the Edmonton and Calgary regions received TKA within the original study timeframe and were eligible for the long-term analysis. Among those contacted, 388 (54%) subjects consented to further participate in the study (See Figure 5.1).

Among the 388 subjects who responded, more participants sourced from the NCP group than the SOC group. This group of responders was comprised of more females than males (59% female, 41% male), with females reporting significantly worse pain and function as reported by the WOMAC and mental health as reported by the SF-36 than their male counterparts at the time of follow-up (See Table 5.1). Most subjects reported having ≤ 2 comorbid conditions (89.1%), with fewer participants reporting ≥ 3 conditions (10.1%). These proportions were also stratified by age categories (≤50, 51-65, 66-75, ≥76), to assess for any trends between reported comorbidities and aging (See Appendix C).

Non-Respondents. At the time of follow-up, 106 subjects were determined to be non-respondents. Of this group, 88 (12%) subjects refused consent to continue with study participation, and 18 (2.4%) subjects were reported as deceased.

At 3-5 years following their TKA, 249 (34%) subjects were lost to follow-up. Among these subjects, 66 (9%) were unable to be contacted due to an incorrect mailing address, while 183 (25%) provided no response to both mail attempts and were unable to be contacted by any other means. These subjects were more likely to have significantly worse preoperative SF-36 MH scores, and worse preoperative WOMAC pain and function scores that those who completed the 3-5 year follow-up. No difference was observed for gender, age or comorbidities between the two groups, although those who were lost to follow-up tended to be younger than respondents ($p = 0.07$) (See Table 5.2).

Changes from Baseline. At 3-5 years post-operatively, respondents were found to have significantly improved WOMAC pain scores and WOMAC function scores from baseline values. Improvements were also seen in SF-36 MH scores; however no changes were found between baseline and follow-up reports of specific comorbidities (See Table 5.3).

Regression Analyses

3-5 Year WOMAC Pain Scores

Univariate Analysis. In a univariate linear regression with 3-5 year WOMAC pain scores as the outcome and a significance level of $p = 0.20$, older age was found to be significantly associated with decreased pain. Higher baseline scores in the WOMAC pain, WOMAC function, and SF-36 MH domains were also associated with greater improvements in pain at the time of follow-up. The presence of back pain at baseline was found to be highly associated with pain, though no other individual comorbidities were significant. In reference to those in a normal BMI classification, participants who were overweight or in any class of obesity were also more likely to have increased pain at 3-5 years postoperatively (See Table 5.4).

Multivariate Analysis. In a multivariate regression analysis for predictors of WOMAC pain scores at 3-5 years post-operatively, older age and presence of back pain remained significant indicators of worse pain levels. Having a BMI classified as overweight and all classes of obesity were also predictors of increased pain. Better postoperative WOMAC pain scores were found to be associated with better preoperative WOMAC pain and SF-36 MH scores. The overall R^2 for the multivariate model was determined to be 0.15 (See Table 5.5).

The model was then tested again with all possible comorbidities summed to one value, rather than extracting certain conditions which were hypothesized to be associated with pain outcomes. In this test of the model, comorbidities were not significant when all possible conditions were summed ($p = 0.10$) and the overall coefficient of determination was reduced ($R^2 = 0.12$).

Confounding and Interaction. Using visual inspection methods, none of the variables removed from the final model were determined to be confounders for included variables. Of the interactions tested, only the interaction between age and baseline WOMAC function scores was significant in the final multivariate model ($\beta = 0.012$, SE = 0.0059; $p = 0.042$) (See Appendix D).

Model Stability. In tests of the model using both forwards and backwards stepwise regression methods, lower baseline WOMAC pain and SF-36 MH scores were associated with improved pain at 3-5 years post-operatively. Increased age and the presence of back pain at the time of operation were significantly associated with worse pain outcomes post-TKA (See Appendix E).

Pairwise correlation tests showed low levels of correlation among independent variables (See Appendix F). In a test of collinearity, however, the interaction variable between age and function was found to have a VIF = 69.16. The baseline WOMAC function variable was found to have a VIF = 61.45. After removing the interaction variable from the model, all remaining variables were found to have a VIF < 10. The interaction term was therefore removed from the final model (See Appendix G).

3-5 Year WOMAC Function Scores

Univariate Analysis. Increasing age, female gender, the presence of lower back pain, and having 3 or more of any comorbidity preoperatively were all significantly associated with worse function in a univariate linear regression with a significance level of $p = 0.20$. Worse function was also found to be predicted by those who were overweight or in any class of obesity. Improved function several years post-operatively was found to be associated with better baseline scores in the WOMAC pain and function domains, and the SF-36 MH component (See Table 5.6).

Multivariate Analysis. In a multivariate regression analysis, increasing age remained as a significant predictor of WOMAC function scores 3-5 years post-operatively. Having a BMI classified as overweight or any class of obesity, as well as the presence of low back pain, were also associated with worse function. Higher baseline WOMAC function and SF-36 MH scores were associated with improved postoperative function scores. The overall R^2 for this multivariate model was identified as 0.19 (See Table 5.7).

The model was then tested again with all possible comorbidities summed to one value, rather than removing and analyzing certain conditions which were hypothesized to be associated with functional outcome. Cumulative comorbidities were not significant in the multivariate model when all possible conditions were summed ($p = 0.12$), and the overall coefficient of determination was again reduced ($R^2 = 0.16$).

Confounding and Interaction. None of the variables removed from the final model were determined as confounders for remaining variables based on visual inspection methods. There were also no significant interactions among the significant variables in the final model (See Appendix H).

Model Stability. When analyzing the model using both forward and backward stepwise regression methods, similar results were found as those found using a purposeful selection technique. This agreement indicates model stability. (See Appendix I).

In a test for collinearity, no variables in the model were found to have a VIF > 10 (See Appendix J).

Secondary Objectives

Physical Activity. At 3-5 years following TKA, participants reported significant increases in the amount of hours spent per day sleeping ($p = 0.003$), sitting ($p < 0.001$), and performing heavy levels of activity ($p < 0.001$). A decrease occurred in the amount of time spent performing activities of slight intensity ($p < 0.001$) while no change occurred in the amount of time engaging in moderate intensity activity ($p = 0.34$) (See Figure 5.2).

At the time of follow-up, more subjects reported performing no walking for exercise and more than 7 hours of walking for exercise or to and from work per week than at baseline. The most notable change in time spent walking per week was observed in the 2-3 hour per week category, which decreased from 241 subjects at baseline to 63 subject at follow-up (See Figure 5.3). At baseline, 28.6% of participants reporting walking less than 2 hours per week, while at 3-5 year post-operatively this proportion increased to 58.1%. This number was also reported once stratified by BMI categories (See Appendix K).

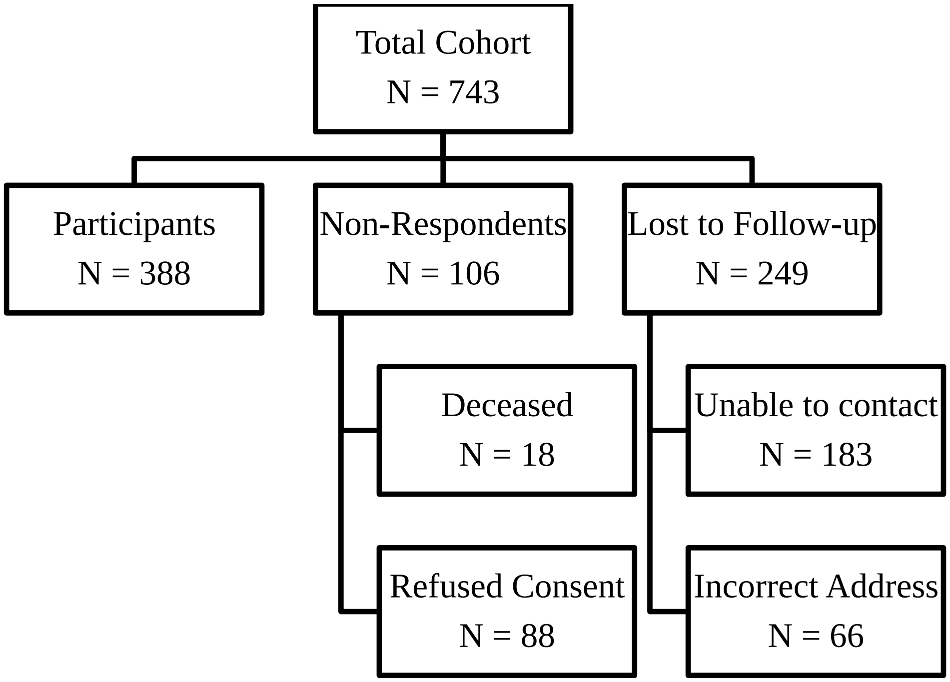

Figure 5.1 Flow chart of 743 TKA recipients.

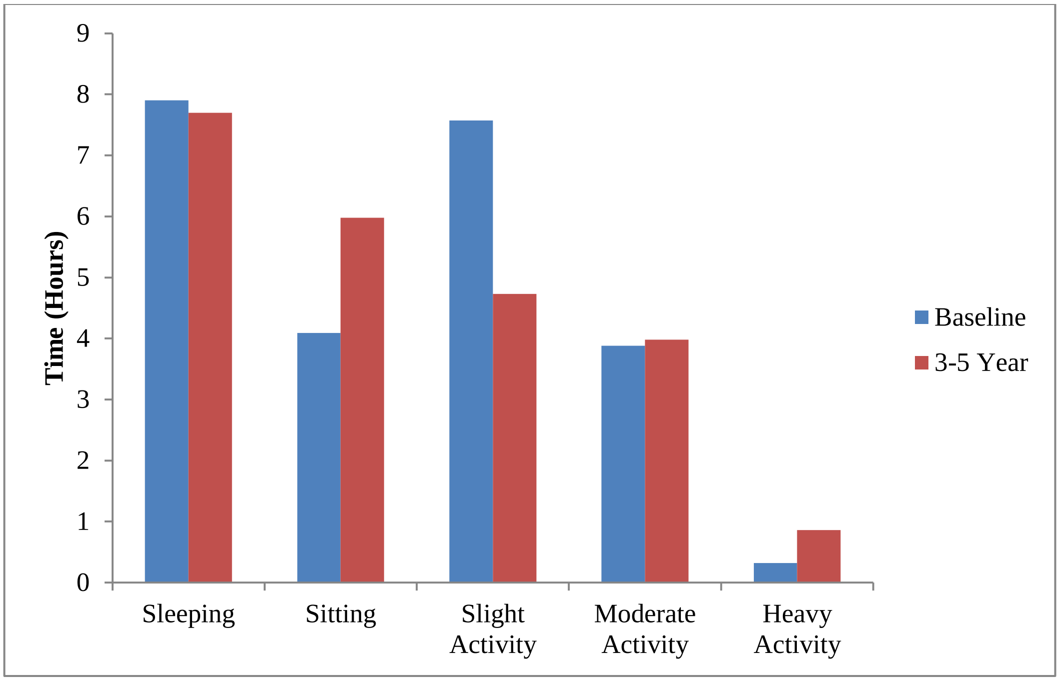

Figure 5.2 Amount of time spent (in hours) performing activities of a given intensity per day.

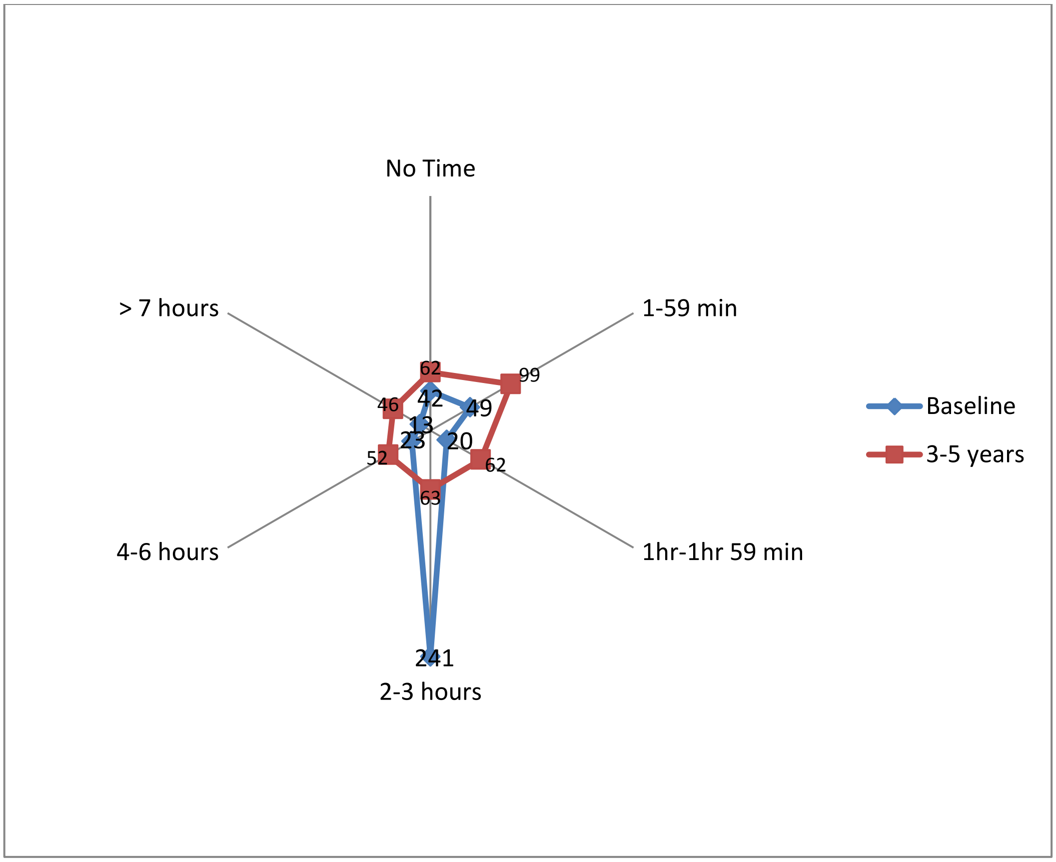

Figure 5.3 Amount of time spent per week walking for exercise or walking to work.

Table 5.1 Baseline demographics for Responders, by gender

Variable	Total (N=388)	Male (N=159)	Female (N=229)	P-Value
Demographics				
Age (SD)	69.0 (9.2)	69.3 (8.4)	68.8 (9.7)	0.67 [a]
Marital Status (%)				
Single	15 (3.9)	3 (1.9)	12 (5.2)	< 0.001 [b]
Married	268 (69.1)	132 (83.0)	136 (59.4)	
Partner/Common law	15 (3.9)	6 (3.8)	9 (3.9)	
Separated	6 (1.6)	4 (2.5)	2 (0.9)	
Divorced	23 (5.9)	8 (5.0)	15 (6.6)	
Widowed	61 (15.7)	6 (3.8)	55 (24.0)	
BMI (SD)	30.4 (5.5)	29.9 (5)	30.7 (5.8)	0.16 [a]
BMI (%)				
≤ 24.9	61 (15.7)	22 (13.8)	39 (17)	0.01
25 - 29.9	140 (36.1)	73 (45.9)	67 (29.3)	
30 - 34.9	113 (29.1)	39 (24.5)	74 (32.3)	
>35	74 (19.1)	25 (15.7)	49 (21.4)	
Group Assignment (%)				
SOC	119 (30.7)	45	74	0.35 [b]
NCP	269 (69.3)	114	155	
Years after surgery				
3	119	56	63	0.17
4	210	81	129	
5	32	10	22	
Comorbidities				
Back Pain (%)	163 (43)	53 (33.5)	110 (49.7)	0.002 [b]
Depression (%)	64 (16.9)	23 (14.6)	41 (18.6)	0.31 [b]
Diabetes (%)	46 (12.2)	22 (14)	24 (10.9)	0.36 [b]
Lung Disease (%)	40 (10.6)	9 (5.8)	31 (14)	0.01 [b]
Smoking Status (%)				
*No**	175 (45.3)	52 (32.9)	123 (53.9)	< 0.001 [b]
Yes, in the past	191 (49.5)	101 (63.9)	90 (39.5)	
Yes, currently	20 (15.2)	5 (3.2)	15 (6.6)	
Cumulative Comorbidities (%)				
≤ 2	349 (89.9)	143 (89.9)	206 (90)	1.0 [b]
≥ 3	39 (10.1)	16 (10.1)	23 (10)	
Outcome Measures				
WOMAC Pain Score (SD)	48.7 (17.5)	52.0 (17.8)	46.4 (17)	0.002 [a]
WOMAC Function Score (SD)	48.9 (17.6)	52.5 (17.5)	46.4 (17.3)	< 0.001 [a]
SF-36 MH Score (SD)	76.4 (15.8)	78.8 (15)	74.8 (16.1)	< 0.001 [a]

[a] Two-Sample Unpaired T-Test
[b] Chi Square Test
Legend: SD= Standard Deviation; SOC = Standard of Care; NCP = New Clinical Pathway

Table 5.2 Baseline demographics for those lost to follow-up, compared with responders

Variable	Included Subjects (N=388)	LTFU (N=249)	P-Value
Demographics			
Age (SD)	69.0 (9.2)	67.6 (10.9)	0.07 [a]
Gender (%)			
Male	159 (41)	99 (39.8)	0.76 [b]
Female	229 (59)	150 (60.2)	
Marital Status (%)			
Single	15 (3.9)	15 (6)	0.89 [b]
Married	268 (69.1)	147 (59)	
Partner/Common law	15 (3.9)	11 (4.4)	
Separated	6 (1.6)	6 (2.4)	
Divorced	23 (5.9)	27 (10.8)	
Widowed	61 (15.7)	43 (17.3)	
BMI (SD)	30.4 (5.5)	30.3 (5.8)	0.81 [a]
BMI (%)			
≤ 24.9	61 (15.7)	43 (17.3)	0.92 [b]
25 - 29.9	140 (36.1)	84 (33.7)	
30 - 34.9	113 (29.1)	74 (29.7)	
>35	74 (19.1)	48 (19.3)	
Group Assignment			
SOC	119 (30.7)	82 (33.1)	0.50 [b]
NCP	269 (69.3)	166 (66.9)	
Comorbidities			
Back Pain (%)	163 (43)	118 (48.4)	0.19 [b]
Diabetes (%)	46 (12.2)	30 (12.2)	0.99 [b]
Lung Disease (%)	40 (10.6)	22 (9.1)	0.52 [b]
Smoking Status (%)			
*No**	175 (45.3)	107 (43.1)	0.09 [b]
Yes, in the past	191 (49.5)	117 (47.2)	
Yes, currently	20 (15.2)	24 (9.7)	
Cumulative Comorbidities (%)			
≤ 2	349 (89.9)	226 (90.8)	0.74 [b]
≥ 3	23 (10.1)	23 (9.2)	
Outcome Measures			
WOMAC Pain Score (SD)	48.7 (17.5)	45.4 (17.5)	0.01[a]
WOMAC Function Score (SD)	48.9 (17.6)	44.3 (17.3)	0.001 [a]
SF-36 MH Score (SD)	76.4 (15.8)	71.1 (18.0)	< 0.001 [a]

[a] Two-Sample Unpaired T-Test
[b] Chi Square Test
Legend: SD= Standard Deviation; SOC = Standard of Care; NCP = New Clinical Pathway

Table 5.3 Changes in baseline and 3-5 year outcomes and comorbidities for responders

Variable	Baseline	3-5 year	P-Value
WOMAC pain score (SD)	48.7 (17.5)	80.2 (19.7)	<0.001 [a]
WOMAC function score (SD)	48.9 (17.6)	77.7 (19.1)	<0.001 [a]
SF-36 MH Score (SD)	76.5 (15.8)	81.4 (14.3)	<0.001 [a]
Back Pain (%)	163 (43)	158 (40.9)	0.6 [b]
Diabetes (%)	46 (12.2)	59 (15.3)	0.2 [b]
Lung Disease (%)	40 (10.6)	48 (12.3)	0.47 [b]
Cumulative Comorbidities (SD)	2.0 (1.34)	2.1 (1.40)	0.008 [a]

[a] Two-Sample Paired T-Test
[b] Chi Square Test
Legend: SD= Standard Deviation

Table 5.4 Univariate analysis for 3-5 year WOMAC pain scores

Variable	β+	SE	P-Value
Demographics			
Age	-0.22	0.11	0.05
Gender (0 = Female)	1.69	2.04	0.41
Marital Status			0.34
*Single**			
Married	-6.34	5.06	0.21
Partner/Common law	-13.85	7.06	0.05
Separated	-4.69	9.41	0.62
Divorced	-11.54	6.40	0.07
Widowed	-8.25	5.52	0.14
BMI (linear)	-0.23	0.18	0.21
BMI (categorical)			0.17
*≤ 24.9**			
25 - 29.9	-4.56	3.01	0.13
30 - 34.9	-6.84	3.12	0.03
>35	-5.46	3.39	0.11
Group Assignment			
*SOC**			
NCP	-1.09	2.18	0.62
Years after surgery			0.29
*3**			
4	-3.57	2.28	0.12
5	-2.04	3.96	0.60
Comorbidities			
Back Pain (0 = No)	-7.61	2.01	<0.001
Diabetes (0 = No)	-0.48	3.11	0.88
Lung Disease (0 = No)	-3.80	3.29	0.25
Smoking Status			0.87
No*			
Yes, in the past	-0.41	2.07	0.85
Yes, currently	-2.46	4.65	0.60
Cumulative Comorbidities (categorical)			0.29
*≤ 2**			
≥ 3	-3.54	3.32	0.29
Outcome Measures			
Baseline WOMAC pain score	0.27	0.06	<0.001
Baseline WOMAC function score	0.26	0.06	<0.001
Baseline SF-36 MH Score	0.25	0.06	<0.001

* = Reference Category; + = Regression Coefficient
Legend: SE= Standard Error; SOC = Standard of Care; NCP = New Clinical Pathway

Table 5.5 Multivariate analysis for 3-5 year WOMAC pain scores

Variable	**β**	**SE**	**P-Value**
Demographics			
Age	-0.38	0.11	0.001
Gender (0 = Female)	-0.35	2.02	0.86
BMI (categorical)			
*≤ 24.9**			
25 – 29.9	-5.80	2.91	0.047
30 – 34.9	-6.45	3.070	0.036
>35	-6.95	3.41	0.04
Group Assignment			
*SOC**			
NCP	-0.95	2.1	0.65
Comorbidities			
Back Pain (0 = No)	-5.26	2.02	0.01
Outcome Measures			
Baseline WOMAC pain score	0.2	0.09	0.03
Baseline WOMAC function score	0.03	0.09	0.71
Baseline SF-36 MH Score	0.16	0.07	0.02

$R^2 = 0.15$
* = Reference Category; $^{+}$ = Regression Coefficient
Legend: SE= Standard Error; SOC = Standard of Care; NCP = New Clinical Pathway

Table 5.6 Univariate analysis for 3-5 year WOMAC function scores

Variable	β +	SE	P-Value
Demographics			
Age	-0.31	0.11	0.004
Gender (0 = Female)	2.91	1.97	0.14
Marital Status			0.37
*Single**			
Married	-5.27	5.06	0.30
Partner/Common law	-11.47	6.96	0.10
Separated	-8.92	9.20	0.33
Divorced	-8.22	6.44	0.20
Widowed	-9.40	5.51	0.09
BMI (linear)	-0.39	0.18	0.03
BMI (categorical)			0.06
≤24.9*			
25 – 29.9	-4.19	2.93	0.15
30 – 34.9	-7.58	3.03	0.01
>35	-7.31	3.29	0.03
Group Assignment			
*SOC**			
NCP	-1.07	2.12	0.62
Years after surgery			0.31
*3**			
4	-3.27	2.2	0.14
5	-3.4	3.86	0.39
Comorbidities			
Back Pain (0 = No)	-8.53	1.95	<0.001
Diabetes (0 = No)	0.73	3.01	0.81
Lung Disease (0 = No)	-4.26	3.22	0.18
Smoking Status			0.61
No*			
Yes, in the past	0.80	2.01	0.69
Yes, currently	-3.61	4.51	0.43
Cumulative Comorbidities (categorical)			0.17
*≤ 2**			
≥ 3	-4.49	3.25	0.17
Outcome Measures			
Baseline WOMAC pain score	0.29	0.05	<0.001
Baseline WOMAC function score	0.34	0.05	<0.001
Baseline SF-36 MH Score	0.27	0.06	<0.001

* = Reference Category; + = Regression Coefficient
Legend: SE= Standard Error; SOC = Standard of Care; NCP = New Clinical Pathway

Table 5.7 Multivariate analysis for 3-5 year WOMAC function scores

Variable	**β^{+}**	**SE**	**P-Value**
Demographics			
Age	-0.46	0.11	<0.001
Gender (0 = Female)	-0.79	1.94	0.69
BMI (categorical)			
*≤ 24.9**			
25 - 29.9	-5.61	2.80	0.046
30 - 34.9	-6.41	2.95	0.03
>35	-8.25	3.25	0.012
Group Assignment			
*SOC**			
NCP	-0.7	2.02	0.74
Comorbidities			
Back Pain (0 = No)	-5.65	1.95	0.004
Lung Disease (0 = No)	-2.26	3.02	0.45
Cumulative Comorbidities (categorical)			
≤ 2*			
≥ 3	-0.52	3.12	0.87
Outcome Measures			
Baseline WOMAC pain score	0.08	0.09	0.36
Baseline WOMAC function score	0.20	0.09	0.02
Baseline SF-36 MH Score	0.15	0.06	0.02

$R^2 = 0.19$
* = Reference Category; $^{+}$ = Regression Coefficient
Legend: SE= Standard Error; SOC = Standard of Care; NCP = New Clinical Pathway

Chapter VI

DISCUSSION

Main Findings

At 3-5 years following a primary TKA, it was found that: increasing age, worse baseline mental health (as determined by the SF-36 MH score), preoperative back pain, increasing BMI, and worse preoperative WOMAC scores in their respective domains were associated with poorer WOMAC pain and functional scores. While similarities were observed for significant variables across the models, slight differences were observed among the magnitude that these variables would affect either pain or function. For example, having a BMI > 35 kg/m^2 was associated with a 6.95 point decrease in 3-5 year WOMAC pain scores and an 8.25 point decrease in 3-5 year WOMAC function scores.

Gender was not a significant predictor of either pain or function at 3-5 years post TKA. Women were found to have worse pain levels and functional status than men pre-operatively, suggesting women should be counselled to seek surgical treatment at earlier stages of joint disease. Although women reported greater levels of pain at baseline, no significance was found at either the univariate or multivariate level of analysis between gender and 3-5 year WOMAC pain scores. The observed difference in baseline pain reports is consistent with that of previous investigations that suggest it is preoperative status rather than gender that has an impact on postoperative pain and function (74, 78-80).

Cumulative comorbidities (as assessed as a dichotomous variable of ≤ 2 and ≥ 3 conditions) were not significantly associated with 3-5 year pain at the univariate level analysis. A significant association was found in the univariate analysis for 3-5 year function; however significance was not maintained in the multivariate model. These findings contribute to the existing heterogeneity of evidence surrounding cumulative comorbidities as a risk factor for worse postoperative pain and functional status.

It is possible that the lack of agreement between the present findings and those from previous investigations are due to varying methods of measuring comorbidities. Those studies using the Charlson Comorbidity Index had greater reports of significance for subjects with more than 2 conditions at the time of follow-up. (74, 79) Until a consensus is reached regarding a methodology for measuring comorbidities, interpretation of results and translation across studies will remain difficult.

For use in this study, cumulative comorbidities were calculated by summing all comorbidities reported, excluding those to be analyzed on a specific level. As such, back pain, lung disease, and diabetes are not included in the cumulative score. This calculation method was chosen to ensure that specific comorbidities that were hypothesized to have the most significant effects were not masked by being included on the cumulative level. To assess whether the inclusion of these three specific comorbidities would affect the significance of the cumulative variable, the model was tested once with their inclusion in the summed variable and once without. Cumulative comorbidities were not significant in either the multivariate pain or function models when all conditions were summed, and both coefficients of determination were reduced. This information illustrates that summing comorbidities may reduce the validity of the model by masking more important variables.

The final coefficients of determination for both the multivariate pain (R^2=0.15) and function (R^2=0.19) models were quite low. In one investigation by Fortin et al. (90) assessing the impact of the single variable baseline WOMAC pain scores on WOMAC pain scores 6-months post-TKA, the coefficient of determination was determined to be R^2=0.25. When assessed in the current investigation, the impact of baseline WOMAC pain scores on 3-5 year pain outcomes at the univariate analysis yielded a coefficient of determination of R^2=0.06. Similarly, when Fortin et al. (90) assessed the predictive ability of baseline WOMAC function scores on WOMAC function scores 6-months post-TKA, the predictive ability of this sole variable was quite high (R^2=0.36). When considered at the same level of analysis in the present study, the predictive ability of this single variable on functional outcomes was notably lower (R^2=0.10). Even after accounting for numerous other variables, the coefficient of determination for the final 3-5 year multivariate model did not reach that reported by Fortin et al. (90) at the univariate level at 6-months post-TKA. This comparison suggests that although bio-medical variables are highly significant in predicting outcomes at shorter periods of follow-up (<6 months), they are less significant for predicting outcomes several years following joint replacement. Rather, other variables (e.g. psycho-social variables) may be better indicators of longer term functional status.

Although not available for use in the present study, future investigations should consider adding these determinants to predictive models.

3-5 Year WOMAC Pain Scores

When considered independently, increased age was a significant predictor of worse pain at 3-5 years post-TKA, and this association remained even after gender and other demographic variables were added to the model. It is possible that this association is due to the increasing number of comorbidities found among elderly patients, resulting in increased pain from other sources. This ideology is in contrast to that proposed by Elson and Brenkel (15) who theorized that older TKA patients would have less awareness of knee specific pain due to other more prominent comorbidities. Older patients should be made aware pre-operatively that they are less likely to reach the same level of pain improvement following TKA as their younger counterparts.

When grouped categorically by age, the oldest TKA recipients (>75 years) experienced significantly less improvements in pain than those in the youngest (≤50 years) age group ($p<0.001$). No significant difference was observed between those in the oldest group and any other age category. Notably, the mean change in WOMAC pain scores among the oldest subjects was 28.9 (± 21.5) points. This is well above accepted MCID ranges of 11-22 points. (63, 65, 116) Age, therefore, should not be a mitigating factor for clinicians when deciding the suitability of a patient to receive a TKA, as older patients are likely to report clinically significant improvements in pain several years post-operatively.

Baseline BMI levels were also significant indicators of pain outcomes at both the univariate and multivariate levels of analyses. Previous investigations have focused largely on the association between BMI and functional outcomes, rather than an association with pain outcomes. Resultantly, a comparison across results is difficult. While associations have been found between the two variables at 1 year post-TKA (88), a large cohort study by Singh et al. (117) did not find any association between moderate-severe pain outcomes and BMI at 2 and 5 years post-TKA. One hypothesis regarding why greater BMI held no association to post-TKA pain levels is that heavier patients are less likely to be physically active, thereby reducing the amount of strain placed on the prosthesis. (117) Findings from our study, however, show that subjects who were defined as obese or overweight at baseline had similar weekly walking levels as those who were normal weight. Based on the aforementioned hypothesis, it is possible that pain among overweight and obese individuals in this sample is related to activity levels greater than those among obese subjects from other study samples that were described as more sedentary.

Presence of back pain at baseline was the only specific comorbidity significantly associated with post-TKA pain during univariate analysis, and this variable retained significance in the multivariate model. To date, limited evidence is available addressing the impact of preoperative back pain on long term TKA pain outcomes. Investigations with shorter term follow-up found similar associations between absence of back pain and improved pain outcomes. (74, 93) It is difficult to compare the findings of the present study to findings from previous investigations given that most existing evidence assesses the presence of low back pain while the current investigation inquired about the presence of non-specific back pain. This evidence suggests, however, that it is important to consider management of any back pain prior to TKA to maximize outcomes several years post-operatively. Given that reported proportions of back pain were similar from baseline to 3-5 year follow-up, it is evident that this musculoskeletal condition requires treatment as it affects other aspects of health, and is unlikely to alleviate over time.

In the final multivariate model, preoperative SF-36 MH scores retained significance as an indicator of post-TKA pain. In a similar investigation with shorter follow-up, Lingard et al (79) found worse baseline SF-36 MH scores to be one of the most significant indicators of greater pain at 1-2 years post-TKA. In a later study, Lingard and Riddle (118) assessed the impact of psychological distress on postoperative WOMAC pain scores, and again found that those with worse pre-TKA SF-36 MH scores were likely to have worse pain outcomes. Interestingly, it was found that individuals with worse mental health reported WOMAC pain scores of 3-5 points lower than their non-distressed counterparts. When analyzed at the individual level, these differences in scores are below accepted MCID ranges (63). In the present study, it is important to note that the β value for the SF-36 MH variable was quite low ($\beta = 0.16$, $p = 0.02$). In this instance, even a preoperative improvement of 20 points in MH score would result in only a 3.2 point improvement on post-TKA WOMAC pain scores. Similar to Lingard and Riddle (118), these results would fall below the MCID threshold. In a clinical perspective, this may indicate that only patients with severe baseline MH scores would benefit from preoperative interventions at improving MH status, given that they have the most room for gains in MH scores. A wide range of change for MH scores reflects the opportunity for WOMAC pain scores to reach the MCID level. Given that the baseline SF-36 MH scores were quite high in this study (76.5 ± 15.8); it is difficult to observe these large changes in score, and further work is required to assess this effect.

At the multivariate level of analysis, better baseline WOMAC pain scores were retained in the model as indicators of postoperative pain. Similar findings exist in other investigations with shorter follow-up periods of 3 and 6 months (90), as well as at 2 and 5 years following surgery. (76, 79, 104) The current findings contribute to the limited body of evidence showing this association extends to several years postoperatively. Baseline pain levels should be an indicator for clinicians when setting patient expectations following surgery.

In a comparison of the magnitude of β coefficients between the present findings and other models with earlier points of follow-up, those assessing outcomes at 1 year or less show preoperative pain will result in greater improvements following TKA ($\beta=0.44$). (90) The current investigation found smaller post-operative improvements in pain for each unit increase in pre-operative WOMAC pain score ($\beta=0.20$). This may indicate that preoperative pain status has less impact on change in pain several years after TKA, particularly when compared to its impact on early post-operative measurements. Future investigations may consider continuing to measure these effects longitudinally to see if the magnitude of the β coefficient continues to decrease.

Gender, group assignment, and baseline WOMAC function scores were not significantly associated with 3-5 year WOMAC pain scores in the final multivariate model. Gender and group assignment were not significant at the univariate level analysis; rather they entered the final model as control variables. Baseline WOMAC function score was highly significant in predicting WOMAC pain scores at the univariate level ($p<0.001$); however this variable lost significance in the final model ($p=0.71$). Previous investigations have accepted that the best predictor of an outcome measure's domain is the preoperative score in that same domain, and that significance between other domains is limited, so this finding was not unexpected. (47, 74, 79, 90)

3-5 Year WOMAC Function Scores

Increasing age was shown to be a highly significant predictor of worse functional outcomes at both the univariate and multivariate levels. These findings are similar to other studies with follow-up durations of greater than 1 year. (48, 76) Given that younger individuals are likely to have greater physical demands in their ADL, it may be reasonable to assume that these patients will have the greatest functional benefit following surgical treatment for their diseased joint. Older individuals may experience functional limitations due to other causes, and resultantly will continue to experience negated function following TKA.

All classifications of BMI greater than normal weight were significant predictors of decreased functional status 3-5 years following TKA. The effect of

BMI on TKA function was shown in a negative linear fashion, indicating that there is a graded response in function to increasing body weight. These findings are of benefit to clinicians preoperatively, as patients may be advised that even a slight amount of excess weight (as commonly found among patients in the overweight class) can be detrimental to longer term TKA outcomes. Fewer existing studies have found BMI to be significantly associated with poor functional outcomes following TKA (88, 119), and among these investigations none found the overweight BMI class to be a significant outcome predictor. Overweight and obese patients may experience worse functional status several years post-operatively due to mobility limitations not associated with their knee, or due to the presence of other comorbidities commonly associated with obesity. This evidence counters several previous investigations, which found no association between BMI and function. In these instances it has been hypothesized that the lack of association is due to the sedentary nature of obese individuals, who experience less forces across the joint. (117, 120)

The presence of back pain was highly significant at both the univariate and multivariate levels of analysis. Previous investigations have assessed low back pain rather than non-specific back pain (74, 91-93), and resultantly a comparison of the present findings to those with previous studies is difficult. The generalizability of the current findings is broader than findings from other studies assessing low back pain in specific, as the generic back pain measure would include this specific subset in the overall back pain demographic. An additional limitation for comparison of results is that no other investigations were found assessing the effect of back pain on patient outcomes at greater than 3 years of follow-up. An investigation by Escobar et al. (74) suggested that the WOMAC is more sensitive to the association between back pain and function, given that it measures activities which are affected by back pain rather than the diseased joint alone. These findings suggest the need for preoperative interventions to alleviate back pain to optimize long term functional outcomes.

Baseline SF-36 MH scores were highly significant predictors of 3-5 year WOMAC function scores in the univariate analysis, and retained significance in the final multivariate model. Similar to the problem encountered with measuring patient comorbidities, there is little consistency among measures used to assess mental health among investigations assessing the predictive ability of mental health status on functional outcomes. Other studies using the SF-36 MH score also found poor scores in this domain were highly significant in predicting functional outcomes at 3 months and 1 year post-TKA. (79, 81) Similar results were found among other investigations using different methods of MH assessment, such as testing depression and anxiety specifically. (88, 96, 97) It is possible that the limited functional improvements experienced several years post-TKA are due to patient's early reservations about rehabilitating their joint. A lack of interest in following necessary rehabilitation protocols could translate to longer term deficiencies in function. Resultantly, a patient with poor MH may interpret their functional status to be far worse than another patient with better MH and similar physical abilities.

Baseline WOMAC function scores were also highly significant predictors of 3-5 year WOMAC function scores at the univariate level of analysis, and retained their significance in the multivariate model. These findings are consistent with those found in earlier investigations with shorter follow-up durations (< 1 year) (90, 91, 95) and those assessing outcomes several years post-operatively. (10, 79)

A lack of consistency exists regarding the magnitude of effect that baseline WOMAC function scores can have on post-operative functional scores. Disagreement exists regarding reported β coefficients at models created using outcomes at 6-months follow-up. Fortin et al. (90) found the contribution of baseline WOMAC scores when predicting 6-month outcomes to be greater than the contribution reported by Jones et al. (91) at the same time of follow-up (β=0.61 compared to β=0.28). In the present study, β coefficients were even lower at the time of 3-5 years post-TKA (β=0.20). The decrease in magnitude of the β coefficient over greater duration of follow-up may suggest that the contribution of baseline WOMAC function scores to post-TKA function scores becomes less relevant over time. Given the heterogeneity of β coefficients reported at 6-months follow-up, however, this remains uncertain.

In the final multivariate model: gender, presence of lung disease, and cumulative comorbidities were not significantly associated with functional outcomes. Cumulative comorbidities and the presence of lung disease were borderline significant ($p<0.20$) in the univariate analyses, but did not reach significance when considered in the presence of other variables. Baseline

WOMAC pain score was highly significant at the univariate level of analysis ($p<0.001$); however it did not retain this significance in the multivariate model. It has been previously investigated that the best determinant of post-TKA WOMAC function scores is the pre-TKA measure from the same domain (47, 79, 90), while other domains such as pain levels are less significant. One study did find conflicting results, indicating that pre-operative pain scores predicted functional levels at 5-years post-TKA. However, these results were produced using the KSS as an outcome measure, and resultantly are difficult to compare to the present findings which are based on the WOMAC domains.

Secondary Objective

Physical Activity. At 3-5 years following their TKA, participants tended to be more sedentary overall than compared to their pre-TKA levels of activity. A significant increase in the time spent sitting per day and a significant decrease in the time spent per day performing slight activity was observed among subjects. This information suggests that regardless of receiving treatment for joint disease which may be hindering physical activity before their TKA, subjects are reluctant to resume and increase activity levels following their joint replacement. A significant improvement was reported in the amount of time spent per day performing heavy levels of activity, which increased to slightly more than 0.5 hours per day. While this improvement in levels of heavy activity is notable, it is difficult to generalize this improvement to all TKA recipients, as older subjects may be less likely to engage in higher intensities of activity. Rather, improvements in amount of time spent performing slight or moderate activity may be more beneficial to this population, as these levels of exertion can be sustained for longer periods of time by a larger demographic.

Slightly more people reported no time spent walking per week at 3-5 years following TKA than at baseline. Similarly, slightly more people reported walking more than 7 hours per week at 3-5 years post-TKA than at baseline. Increases were seen in all other walking time categories, with the exception of the 2-3 hours per week category. At baseline, most subjects reported spending 2-3 hours per week walking; however at follow-up this category had the greatest decrement in responses. While some subjects who left this category may be those who later reported increases in time spent walking, they would only comprise a small amount of responders. The decrease in subjects from the baseline 2-3 hour category was so drastic that some participants inevitably would have reported lower amounts of time spent walking at follow-up. Again, this illustrates that there is an increase in sedentary nature among many TKA recipients.

In an earlier assessment on walking activity after THA or TKA, it has been suggested that when assessing how activities affect the wear of a lower joint prosthesis, walking is the most important activity to consider. (121) Investigators suggest that walking should be assessed as a function of use through measured cycles (e.g. number of steps), rather than as a function of time spent performing the activity. When controlling for age it was found that subjects who had undergone THA or TKA performed fewer steps than subjects who had not undergone a TJA. While this does not reflect their change in quantity of steps from preoperative levels, the comparison to healthier controls indicates that TJR is associated with decrements in walking activities. Though the current study assessed walking as a function of time, similar findings in the context of reduced walking levels following TKA were observed.

Although an improvement was shown in daily amounts of heavy activity, the overall trend appears to be an increase in sedentary behaviour as observed by the increase in time spent sitting daily and decrease in slight activity levels. Previous cross-sectional investigations have found that TKA recipients tend to report performing some amount of low to moderate physical activity at 1-5 years post-TKA; however this information has limited generalizability due to baseline physical activity levels not being accounted for. (122,123) Additionally, these investigations did not assess the duration for which these activities were performed; rather only the intensities were assessed.

Given the overall increase in sedentary activity following TKA, a greater emphasis may be necessary post-operatively on the importance of maintaining an active lifestyle. Post-operatively, TKA recipients may be hesitant to resume pre-operative activity levels for fear of placing too much strain on the prosthesis. While reduced activity levels may be intended as a protective mechanism, existing evidence suggests a negative effect. As indicated by Kuster (124), physical activity following joint replacement is necessary not only for the maintenance of overall health, but for the health of the surrounding bone. Increased activity is hypothesized to improve bone quality surrounding the prosthesis, thereby reducing the risk of loosening and its associated complications. While some existing literature surrounding physical activity and

TKA outcomes has focused on pre-operative exercise interventions, an emphasis should also be placed on longer term post-operative exercise regimens to assist in joint rehabilitation and overall maintenance of the prosthesis and surrounding bone. Given that younger patients are receiving TKA, improved physical activity and lifestyle methods may assist in the longevity of the joint replacement. Increased patient education on the importance of maintaining or improving activity levels post-operatively might be considered as one solution to the problem of increased sedentary behaviour.

Strengths of the Study

This study involved prospectively collected data from a large population cohort, consisting of subjects who received treatment from two large urban cities. Patients serviced in these areas included those from both urban and rural settings. This population also captured a wide demographic of ages, preoperative health statuses, pain levels, and functional abilities. These factors increase the generalizability of our study. The data utilized for this investigation was a comprehensive set of medical and patient demographics, allowing for a rich analysis to be performed.

Outcomes were assessed using the WOMAC, a measurement tool that has repeatedly been shown to have high reliability and validity. The WOMAC has also been shown to be responsive to clinical change across patient populations, allowing for a great level of confidence in the improvements observed across reported outcomes. The SF-36, which was used to assess participant MH status, is another measure used which has also been repeatedly validated.

Using risk adjusted methods, the impact of multiple comparisons at the level of $p<0.05$ was also managed. Using a wide inclusion criteria of $p<0.20$ at the univariate level allowed for variables that may not have been independently significant to still be considered in the presence of other characteristics. Also, given that that population for this analysis was larger, risk adjustment at the multivariate level allowed for certainty that identified variables were in fact significant, and not due to the large sample size. Given the large number of inferences being made, a risk adjusted analysis was necessary.

Several attempts were made to contact those who did not respond to the first mail-out at follow-up. These attempts ensure that as many participants as possible were accounted for in the analyses, and that those who were not able to be contacted were accurately allocated to the lost to follow-up cohort.

Limitations of the Study

The primary limitation to the present study is that a 54% follow-up rate was achieved. The proportion falls at the lower end of the response rate spectrum, and resultantly may represent a limited ability of the data to accurately reflect the results of the entire population under study. While there is no agreed standard as to what response rate is deemed satisfactory or high, a response rate of approximately half the intended target has been accepted as low. (125) One possible reason for low participant response rates is that fewer subjects who were allocated to the SOC group completed the questionnaires at 3-5 years compared to those in the NCP group. These SOC subjects may have declined to further participate or respond as they were dissatisfied with the initial time waiting for surgery, and limited availability for follow-up several years post-TKA. These subjects may not have seen further participation as being beneficial to them, whereas participation in the preoperative phase may have meant the benefit of improved time to surgery under a new care plan. It is also possible that subjects declined to further participate or reply due to the apparent length of the questionnaire. In order to increase subject response rates, future investigations might aim to reduce the length of the questionnaire supplied. Questionnaires might also be administered through other methods, such as providing participants the option of responding either using traditional paper-based format or using an e-mail format. The option to respond electronically may appeal to younger members of the cohort, or to those who find traditional mail responses to be inconvenient. One investigation assessing methods to improve non-response rates found greater success when a second method of contact (email) was used to reach subjects who did not reply to primary contact attempts. (126)

Subjects utilized for this study were those who were participants of the Alberta New Arthroplasty Model pilot project. These patients were randomly assigned to treatment groups, and results of this study show that treatment group did not significantly affect patient outcomes. It must be considered, however, whether patients who declined participation in the early pilot project differed from those who consented. Significant differences were found between responders and those who were lost to follow-up. Responders were likely to have better baseline WOMAC pain and function scores, as well as greater SF-36 MH scores. Though statistical significance wasn't reached, younger age among non-responders was approaching significance ($p<0.07$).

Although the WOMAC has been shown to be highly valid, reliable, and sensitive to change, it is problematic in that it asks respondents to assess their pain and function with respect to their diseased knee. Some individuals may respond on a more global health level, rather than in regard to their specific joint. As a result, it may be uncertain whether some respondents are reporting their pain and functional status according to the joint, or due to another underlying condition.

The measurement of comorbidities among existing investigations is not consistent, and no standard for comparison of comorbidities exists. Although the current data set captures a wide set of conditions, its categories are not homogenous with other studies. For this reason, certain difficulties arise such as interpreting whether patient reports of back pain are specific to low back or other regions. As well, it is difficult to interpret whether patient reports of depression and anxiety in the questionnaire are clinical diagnoses or patient interpretations of their present mental state. In this instance, the SF-36 MH score was used to control for uncertainty of patient reported MH status.

The final coefficients of determination for both the multivariate pain (R^2=0.15) and function (R^2=0.19) models were quite low. This indicates that the included variables are capable of accounting for 15% of the pain outcomes and 19% of the function outcomes at 3-5 years post-TKA. It is of importance to note that the present model includes variables which are mainly medical, and fails to assess other psycho-social aspects. This information may indicate that longer term outcomes are less dependent on physiological variables. Low R^2 values may also be a result of low participant follow-up at 3-5 after surgery. A comparison to future investigations with similar design and a greater proportion of responders may be beneficial in determining whether the present low coefficients of determination are related to selected variables or response rates. Future research may also consider the impact of including psycho-social variables in predictive models for longer term TKA pain outcomes.

Chapter VII

CONCLUSIONS AND RECOMMENDATIONS

Conclusion

The findings of this study indicate that: increasing age, worse baseline WOMAC pain score, worse baseline SF-36 MH score, presence of back pain, and having a BMI in any category above normal weight significantly predict worse WOMAC pain scores at 3-5 years post-TKA. When considering 3-5 year WOMAC function scores: increasing age, worse baseline WOMAC function score, worse baseline SF-36 MH score, presence of back pain, and having a BMI in any category above normal weight predict worse outcomes.

These findings contribute to the existing body of evidence which is inconclusive or limited in findings for outcomes at a follow-up period of several years post-TKA. The results of the multivariate models, particularly the low R^2 values, suggest that the current variables being considered at baseline as predictors of TKA outcomes are more pertinent to shorter term follow-up. Over longer durations, medically based variables may have less of an impact on patient outcomes. Rather, more psycho-social variables should be considered for predicting longer-term outcomes.

Based on the identified risk factors, pre-operative interventions may be set to reduce BMI, alleviate back pain, and improve patient MH status. Patients should be made aware of the increased risk of worse outcomes in the event that they do not consider improving these variables. Patients with worse baseline pain and functional status should have appropriate expectations for their TKA outcomes, given their pre-operative status.

Recommendations

Clinical.

- Women should be encouraged to seek surgical treatment for their degenerated joint at earlier disease stages, as they present as significantly worse than males in terms of pain and function at baseline.
- Mental health status of a patient should be identified pre-operatively, and interventions should be offered to improve the MH status of those identified as having poor mental health.
- Patients should be educated on weight reduction strategies pre-operatively. Post-TKA, patients should receive counselling on appropriate weight management strategies to sustain a healthy BMI long-term.
- Patients with worse baseline WOMAC function scores should have their expectations appropriately set regarding the level of functional improvement they are likely to experience up to several years following their TKA.
- Patients with worse baseline WOMAC pain scores should have their expectations appropriately set regarding the level of improvement in pain they are likely to experience up to several years following their TKA.

For research.

- A standardized tool for measuring comorbidities should be implemented across investigations to allow for homogeneity and better comparison of results.

- More investigations are necessary which assess the association of patient demographics to long-term (>3 years) patient outcomes in the domains of pain and function following TKA. Specifically, these should include the WOMAC as an outcome measure, given that it is validated, economical, and widely used. These investigations should also attempt to use larger sample sizes (n > 100) to increase the detection of significant outcomes.
- Future investigations assessing the association between patient demographics and long-term (>3 years) patient outcomes in the domains of pain and function should include psycho-social demographics as independent variables.
- Investigations using statistical modelling to predict patient outcomes should utilise the method of multivariate linear regression, rather than logistic regression techniques.

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Appendix A

CONSENT FORM

Title of Project: A Randomized Controlled Prospective Study to Examine the Efficacy of a new Evidence Based Arthroplasty Care Model versus the Existing Conventional Approach for Patients with Severe Degenerative Joint Disease (DJD) of the Hip or Knee

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Please circle your answers:

Do you understand that you have been asked to be in a research study? Yes No

Have you read and received a copy of the attached information sheet? Yes No

Do you understand the benefits and risks involved in taking part in this research study? Yes No

Have you had an opportunity to ask questions and discuss this study? Yes No

Do you understand that you can quit taking part in this study at any time? Yes No

Has how we will keep the data confidential been explained to you? Yes No

Do you understand who will have access to your health information? Yes No

Do you wish to donate your discarded tissue at time of revision surgery if applicable? Yes No

I agree to take part in this study. Yes No

Signature of Research Participant	Printed Name	Date
Patient Healthcare Number	Daytime Phone	Additional Phone
Signature of Investigator/Delegate	Printed Name	Date
Witness Signature	Printed Name	Date

INFORMATION SHEET

Title of Project: A Randomized Controlled Prospective Study to Examine the Efficacy of a new Evidence Based Arthroplasty Care Model versus the Existing Conventional Approach for Patients with Severe Degenerative Joint Disease (DJD) of the Hip or Knee: **Long-Term Follow-up**

Principal Investigators:

Dr. Lauren Beaupre, Departments of Surgery and Physical Therapy, University of Alberta, Phone: (780) 407-6848.
Dr. Cy Frank, Department of Surgery, University of Calgary, Phone: (403) 220-6881.
Dr. Bill Johnston, Orthopedic Surgeon, University of Alberta, Phone: (780) 407-6848.

Background: Degenerative joint disease (DJD) affects over ten percent of the Alberta population. Seventy percent of patients over the age of 70 have been identified as having radiographic evidence of OA and arthritis represents the second most common reason for a visit to a physician. Hip and knee replacements have been recognized as one of the most effective surgical interventions in the management of this condition.

You agreed to participate in a study that was looking at outcomes after total joint replacement. You were randomized into one of two study groups. Group A (the intervention group) received and continue to receive care for their hip or knee in a specialized 'hip and knee' clinic. Group B (the control group) received their treatment as per usual standard of care. You completed mailout questionnaires before your surgery and at 3 months and 1 year after your surgery. At the end of 1 year, all patients in both groups began to receive their ongoing care at the hip and knee clinics in Edmonton, Calgary or Red Deer.

Purpose of Research: To follow the patients who were a part of the New Arthroplasty Care Model study and see how they do between 1 and 10 years after their total joint replacement surgery.

Procedures:

You are now at least 3 years after your total joint replacement surgery. We would like to ask you similar questions as you answered in the first year after your surgery. We have reduced the number of questionnaires that you need to complete. If you agree to participate in this part of the follow-up study, data will be collected from your medical charts, interviews, and from data maintained within the databases at Alberta Health and Wellness. Your Alberta Health Care Number is needed so that the study can obtain your information from the databases in Alberta Health and Wellness. Interviews and data collection will take place when this follow-up study begins (approximately 3 years after surgery) and again every 2 years after that for a total of 10 years after your surgery. If you require another joint replacement surgery on the same joint ('re-do"), we will follow-up with you annually to see how you do after your revision or redo joint replacement.

Confidentiality: All information captured during the data analysis process will comply with the Health Information Act and will be stored and maintained in a strictly confidential manner. You will maintain the same study ID number as in the first study. All data will be secured and only grouped non-identifiable information will be released in reports, publications or presentations.

Benefits: By participating in this study, you are providing the orthopaedic surgeons and other health professionals information to help them make decisions regarding the best model of care for patients with degenerative joint disease of the hip or knee in Alberta. The results of this study will help to improve care and quality of life for patients with hip and knee arthritis in Alberta.

Withdrawal from the study: You are free to withdraw at any time without risk of adverse consequences. Your decision to withdraw from the study will not hinder your subsequent medical treatments.

Consent Form: If you are comfortable with the above information and wish to participate in the study, please complete the consent form. Your signature on this form indicates that you have understood to your satisfaction the information regarding participation in the project and agree to participate as a subject. If you have any concerns about your rights as a study participant, you may contact the Patient Relations Office of Capital Health at (780) 342-1040. If you have any questions or concerns about any aspect of the study, please contact Dr. Lauren Beaupre, Co-Principal Investigator, Phone: (780) 407-6848, Dr. Bill Johnston, Co-Principal investigator, Phone: (780) 407-6848 or Cy Frank, (University of Calgary), Phone: (403) 220-6881.

You will be given a copy of this form to keep for future reference.

Appendix B

ALBERTA BONE & JOINT HEALTH INSTITUTE

Patient Questionnaire

IMPORTANT POINTS TO REMEMBER WHEN COMPLETING THE QUESTIONNAIRE

- This package is double sided – please complete questions on both sides of the paper
- Please complete **EVERY** question
- Please mail back the completed questionnaire in the postage paid envelope as soon as possible
- If you have any questions please call 1-866-670-0886

Last Name: ____

First Name: ____

Middle Initial: ____

Orthopaedic Surgeon: __________________________________

Today's Date: __________ / _________ / __________
Day Month Year

Preferred Mailing Address and Phone Number:

Address:
____

____

City: _________________ Prov.: ____________Postal Code:_________________

Phone Number: ____________________________________

Alternative Phone Number: ___________________________

E-mail:____

How would you prefer to be contacted for future follow-ups?

☐ EMAIL ☐ TELEPHONE ☐ MAIL

JOINT REPLACEMENT HISTORY

In the past, have you ever had surgery for the following JOINT REPLACEMENTS

SHOULDER REPLACEMENT

☐ YES ☐ NO If Yes, ☐ LEFT ☐ RIGHT ☐ BOTH Year(s): _______________

HIP REPLACEMENT

☐ YES ☐ NO If Yes, ☐ LEFT ☐ RIGHT ☐ BOTH Year(s): _______________

KNEE REPLACEMENT

☐ YES ☐ NO If Yes, ☐ LEFT ☐ RIGHT ☐ BOTH Year(s): _______________

OTHER JOINT REPLACEMENT

☐ YES ☐ NO If Yes, ☐ LEFT ☐ RIGHT ☐ BOTH Year(s): _______________

OTHER HEALTH INFORMATION

Have you ever smoked cigarettes?

☐ NO, NEVER

☐ YES, IN THE PAST

YEAR QUIT: ____________

APPROXIMATE NUMBER SMOKED EACH DAY: _______

APPROXIMATE NUMBER OF YEARS YOU SMOKED: _______

☐ YES, I CURRENTLY SMOKE

YEAR STARTED: ____________

APPROXIMATE NUMBER OF CIGARETTES YOU SMOKE PER DAY: _______

Current alcohol consumption

What type and amount of alcoholic beverage(s) do you consume in an average WEEK? ☐ N/A ☐ PREFER NOT TO SAY

	YES	NO	AMOUNT CONSUMED
BEER	☐	☐	BOTTLES _________ CANS _________ GLASSES _________
WHITE WINE	☐	☐	GLASSES _________
RED WINE	☐	☐	GLASSES _________
LIQUOR	☐	☐	COCKTAILS _________ HIGHBALLS _________
OTHER	☐	☐	____

Do you have any of the following problems?

NOTE: If you receive any medications for the following health conditions, please ensure they are listed in the medication table on **PAGE 3**

1. HEART DISEASE (e.g. congestive heart failure, heart murmur, valve disease).

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ______________________________

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

2. HIGH BLOOD PRESSURE

☐ YES ☐ NO

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

3. LUNG DISEASE (e.g. ASTHMA, COPD, EMPHYSEMA)

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ______________________________

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

4. DIABETES

☐ YES ☐ NO IF **YES**, YEAR OF ONSET: ______________

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

5. STOMACH ULCERS OR GASTROINTESTINAL DISEASE (e.g., Crohn's disease, irritable bowel syndrome)

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ______________________________

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

6. LIVER DISEASE (e.g., hepatitis, cirrohsis)

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ______________________________

If **YES**, Do you currently receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

7. KIDNEY DISEASE

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ____

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Are you currently receiving dialysis? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

8. ANEMIA OR OTHER BLOOD DISEASES

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ____

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

9. CANCER

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ____

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

10. DEPRESSION OR ANXIETY

☐ YES ☐ NO

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

11. BACK PAIN

☐ YES ☐ NO

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

12. THYROID DISEASE

☐ YES ☐ NO IF **YES**, PLEASE SPECIFY: ____

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

13. OTHER HEALTH PROBLEMS (please write in)

☐ YES ☐ NO OTHER PROBLEMS IF **YES**, PLEASE SPECIFY: ______________________

If **YES**, Do you <u>currently</u> receive treatment for it? ☐ YES ☐ NO

Does it limit your activities? ☐ YES ☐ NO

QUALITY OF LIFE INFORMATION

The questions on the next 6 pages ask you about your GENERAL HEALTH, i.e., not only your hip or knee condition. Please answer them with consideration of your overall health.

In general, how would you say your health is (please check one box)?

☐ EXCELLENT ☐ VERY GOOD ☐ GOOD ☐ FAIR ☐ POOR

Compared to one year ago, how would you rate your health in general now? (please check one box only)

☐ MUCH BETTER THAN ONE YEAR AGO ☐ SOMEWHAT BETTER THAN ONE YEAR AGO

☐ ABOUT THE SAME AS ONE YEAR AGO ☐ SOMEWHAT WORSE THAN ONE YEAR AGO

☐ MUCH WORSE THAN ONE YEAR AGO

The following questions are about the activities you might do in a typical day. Does your health limit you in the following activities? If so, by how much? (please check mark "√" ONE box for each question)

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Lifting or carrying groceries	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Climbing **several** flights of stairs	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Climbing **one** flight of stairs	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Bending, kneeling, or stooping	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Walking **more** than one mile	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Walking **several** blocks	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Walking **one** block	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL
Bathing or dressing yourself	☐ LIMITED A LOT	☐ LIMITED A LITTLE	☐ NOT LIMITED AT ALL

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Cut down on the amount of time you spent on work or other activities?	☐ YES	☐ NO
Accomplished less than you would like?	☐ YES	☐ NO
Were limited in the kind of work or other activities?	☐ YES	☐ NO
Had difficulty performing the work or other activities (for example, it took extra effort)?	☐ YES	☐ NO

During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of any emotional problems (for example, feeling depressed or anxious)?

Cut down on the amount of time you spent on work or other activties?	☐ YES	☐ NO
Accomplished less than you would like?	☐ YES	☐ NO
Didn't do work or other activities as carefully as usual?	☐ YES	☐ NO

During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups? (please check one box only)

☐ NOT AT ALL ☐ SLIGHTLY ☐ MODERATELY ☐ QUITE A BIT ☐ EXTREMELY

How much physical pain have you had during the past 4 weeks? (please check one box only)

☐ NONE ☐ VERY MILD ☐ MILD ☐ MODERATE ☐ SEVERE ☐ VERY SEVERE

During the past 4 weeks, how much pain interfered with your normal work, including both work outside the home and housework? (please check one box only)

☐ NOT AT ALL ☐ SLIGHTLY ☐ MODERATELY ☐ QUITE A BIT ☐ EXTREMELY

These questions are about how you feel and how things have been with you during the past 4 weeks. Please circle only one number per question.

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	1	2	3	4	5	6
Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and blue?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities, like visiting friends or relatives etc.?
Please check one box only.

☐ ALL OF THE TIME ☐ MOST OF THE TIME ☐ SOME OF THE TIME ☐ A LITTLE OF THE TIME ☐ NONE OF THE TIME

How TRUE or FALSE is each of the following statements for you?

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
I seem to get sick a little easier than other people	1	2	3	4	5
I am as healthy as anybody	1	2	3	4	5
I expect my health to get worse	1	2	3	4	5
My health is excellent	1	2	3	4	5

The questions on the next 3 pages are specific to your HIP OR KNEE condition.

The following questions concern the amount of pain you have experienced due to arthritis in your HIP/KNEE joint(s). For each situation please enter the amount of **PAIN** experienced in the last 48 hours. Please check **ONE BOX ONLY** for each question.

Walking on a flat surface

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Going up or down stairs

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

At night while in bed

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Sitting or lying

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Standing upright

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

The following questions concern the amount of joint stiffness (not pain) you have experienced due to arthritis in your HIP/KNEE joint(s). Stiffness is a sensation of restriction or slowness in the ease with which you move your hip/knee joint. For each situation please enter the amount of **STIFFNESS** experienced in the last 48 hours. Please check **ONE BOX ONLY** for each question.

How severe is your stiffness after first wakening in the morning?

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

How severe is your stiffness after sitting, lying or resting later in the day?

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

The following questions concern your **PHYSICAL FUNCTION**. By this we mean your ability to move around and look after yourself. For each of the following activities, please indicate the degree of difficulty you have experienced in the last 48 hours due to your arthritis in your HIP/ KNEE joint(s). Please check **ONE BOX ONLY** for each question.

Descending stairs

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Ascending stairs

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Rising from sitting

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Standing

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Bending to the floor

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Walking on a flat surface

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Getting in or out of a car

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Going shopping

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Putting on socks or stockings

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Rising from bed

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Taking off socks or stockings

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Lying in bed

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Getting in or out of a bath

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Sitting

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Getting on or off a toilet

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Heavy domestic duties

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

Light domestic duties

☐ NONE ☐ MILD ☐ MODERATE ☐ SEVERE ☐ EXTREME

PHYSICAL ACTIVITY INFORMATION

INSTRUCTIONS: This set of questions asks you for your views about your physical activity. Your answers to these questions should reflect your level of activity in a **TYPICAL WEEK.** If you are unsure about how to answer a question, please give the best answer you can.

REST AND ACTIVITY FOR A TYPICAL DAY (Please note that your answers should total 24 hours)	**Approximate number of hours per day**
THE NUMBER OF HOURS THAT YOU TYPICALLY SLEEP	________
THE NUMBER OF HOURS YOU ARE TYPICALLY SITTING	________
THE NUMBER OF HOURS WITH SLIGHT ACTIVITY (e.g. standing or walking)	________
THE NUMBER OF HOURS WITH MODERATE ACTIVITY (e.g. housework, vacuum, dusting, yard chores, climbing stairs, light sports such as golf or bowling)	________
THE NUMBER OF HOURS WITH HEAVY ACTIVITY (e.g. heavy yard work such as chopping or stacking wood, intensive sports such as jogging or swimming)	________
TOTAL HOURS	24

What is your normal walking pace outdoors? (Please check one box only)

- ☐ UNABLE TO WALK
- ☐ EASY, CASUAL, SLOW
- ☐ NORMAL, AVERAGE
- ☐ BRISK PACE
- ☐ VERY BRISK PACE
- ☐ UNKNOWN

Approximately how many flights of stairs (not steps) do you climb daily? (estimated 10 steps per flight) Please check one box only.

- ☐ NO FLIGHTS
- ☐ 1 - 2 FLIGHTS
- ☐ 3 - 4 FLIGHTS
- ☐ 5 - 9 FLIGHTS
- ☐ 10 - 14 FLIGHTS
- ☐ MORE THAN 15 FLIGHTS
- ☐ UNKNOWN

During the PAST YEAR what was you average time PER WEEK spent in each of the following activities? Please check one box only for each activity.

Walking for exercise or walking to work

☐ NO TIME	☐ 1 - 4 MINUTES	☐ 5 - 19 MINUTES	☐ 20 - 59 MINUTES	☐ I HOUR
☐ 1 - 1.5 HOURS	☐ 2 - 3 HOURS	☐ 4 - 6 HOURS	☐ 7 - 10 HOURS	☐ MORE THAN 11 HOURS

Jogging (slower than a 10 minute mile)

☐ NO TIME	☐ 1 - 4 MINUTES	☐ 5 - 19 MINUTES	☐ 20 - 59 MINUTES	☐ I HOUR
☐ 1 - 1.5 HOURS	☐ 2 - 3 HOURS	☐ 4 - 6 HOURS	☐ 7 - 10 HOURS	☐ MORE THAN 11 HOURS

Running (10 minutes per mile or faster)

☐ NO TIME	☐ 1 - 4 MINUTES	☐ 5 - 19 MINUTES	☐ 20 - 59 MINUTES	☐ I HOUR
☐ 1 - 1.5 HOURS	☐ 2 - 3 HOURS	☐ 4 - 6 HOURS	☐ 7 - 10 HOURS	☐ MORE THAN 11 HOURS

Bicycling (including stationary bike)

☐ NO TIME	☐ 1 - 4 MINUTES	☐ 5 - 19 MINUTES	☐ 20 - 59 MINUTES	☐ I HOUR
☐ 1 - 1.5 HOURS	☐ 2 - 3 HOURS	☐ 4 - 6 HOURS	☐ 7 - 10 HOURS	☐ MORE THAN 11 HOURS

Tennis, squash or racketball

☐ NO TIME	☐ 1 - 4 MINUTES	☐ 5 - 19 MINUTES	☐ 20 - 59 MINUTES	☐ I HOUR
☐ 1 - 1.5 HOURS	☐ 2 - 3 HOURS	☐ 4 - 6 HOURS	☐ 7 - 10 HOURS	☐ MORE THAN 11 HOURS

Lap swimming

- [ ] NO TIME
- [ ] 1 - 4 MINUTES
- [ ] 5 - 19 MINUTES
- [ ] 20 - 59 MINUTES
- [ ] I HOUR
- [ ] 1 - 1.5 HOURS
- [ ] 2 - 3 HOURS
- [ ] 4 - 6 HOURS
- [ ] 7 - 10 HOURS
- [ ] MORE THAN 11 HOURS

Other aerobic exercise (aerobic dance, skiing, stair machine, rowing)

- [ ] NO TIME
- [ ] 1 - 4 MINUTES
- [ ] 5 - 19 MINUTES
- [ ] 20 - 59 MINUTES
- [ ] I HOUR
- [ ] 1 - 1.5 HOURS
- [ ] 2 - 3 HOURS
- [ ] 4 - 6 HOURS
- [ ] 7 - 10 HOURS
- [ ] MORE THAN 11 HOURS

Lower intensity exercise (yoga, pilates, stretching)

- [ ] NO TIME
- [ ] 1 - 4 MINUTES
- [ ] 5 - 19 MINUTES
- [ ] 20 - 59 MINUTES
- [ ] I HOUR
- [ ] 1 - 1.5 HOURS
- [ ] 2 - 3 HOURS
- [ ] 4 - 6 HOURS
- [ ] 7 - 10 HOURS
- [ ] MORE THAN 11 HOURS

Other vigorous exercise (lawnmowing)

- [ ] NO TIME
- [ ] 1 - 4 MINUTES
- [ ] 5 - 19 MINUTES
- [ ] 20 - 59 MINUTES
- [ ] I HOUR
- [ ] 1 - 1.5 HOURS
- [ ] 2 - 3 HOURS
- [ ] 4 - 6 HOURS
- [ ] 7 - 10 HOURS
- [ ] MORE THAN 11 HOURS

Weight training including free weights or weight machines

- [ ] NO TIME
- [ ] 1 - 4 MINUTES
- [ ] 5 - 19 MINUTES
- [ ] 20 - 59 MINUTES
- [ ] I HOUR
- [ ] 1 - 1.5 HOURS
- [ ] 2 - 3 HOURS
- [ ] 4 - 6 HOURS
- [ ] 7 - 10 HOURS
- [ ] MORE THAN 11 HOURS

Please list any other activities that you do that are not listed above, and the approximate time you spend per week participating in these activities

- [ ] I do not participate in any other activities

Activity	**Time per week**	**Duration** (approximate number of hours per session)

Appendix C

Number (%) of patients by age in cumulative comorbidities categories

	Age			
Cumulative Comorbidities	**≤ 50 years**	**51-65 years**	**66-75 years**	**≥ 76 years**
≤ 2	31 (100)	150 (90.51)	83 (89.25)	84 (85.71)
≥ 3	0	15 (9.09)	10 (10.75)	14 (14.29)

Appendix D

Interactions with 3-5 year WOMAC pain score as outcome

Interaction	β	SE	P-value
Comorbidities * SF-36 MH Score (≤ 2 comorbidities = 0)	-0.11	0.18	0.53
WOMAC Pain Score * SF-36 MH Score	0.005	0.003	0.12
BMI * WOMAC Function Score			
≤24.9ǂ			
25 - 29.9	0.18	0.15	0.23
30 - 34.9	0.074	0.16	0.65
>35	0.06	0.20	0.76
BMI * WOMAC Pain Score			
≤24.9ǂ	0.10	0.15	0.50
25 - 29.9	0.11	0.16	0.52
30 - 34.9	0.05	0.18	0.77
>35			
Gender * WOMAC Pain Score	0.01	0.11	0.91
Gender * WOMAC Function Score	-0.12	0.11	0.27
Age * WOMAC Pain Score	0.007	0.006	0.20
Age * WOMAC Function Score	0.012	0.006	0.04
Age * Gender	0.12	0.22	0.59

ǂ Reference group

Appendix E

Forward and backward stepwise regression for 3-5 year WOMAC pain scores

	Forward Stepwise Regression			Backward Stepwise Regression		
Variable	β^+	SE	P-Value	β^+	SE	P-Value
WOMAC pain score	0.2	0.06	<0.001	0.22	0.06	<0.001
SF-36 MH score	0.17	0.07	0.02	0.17	0.07	0.02
Age	-0.35	0.11	0.002	-0.35	0.11	0.002
Back pain	-5.31	2.12	0.01	-5.32	2.12	0.01

Forward stepwise regression R^2 = 0.11
Backward stepwise regression R^2 = 0.11
$^+$ = Regression Coefficient
Legend: SE= Standard Error

Appendix F

Pairwise correlation between all independent variables for model consideration

	WOMAC pain	WOMAC function	Age	Back Pain	Diabetes	Lung Disease
WOMAC pain	1.000					
WOMAC function	0.797	1.000				
Age	0.120	0.055	1.000			
Back Pain	-0.135	-0.131	-0.011	1.000		
Diabetes	0.007	-0.043	-0.032	0.001	1.000	
Lung Disease	-0.022	-0.037	0.047	0.102	0.002	1.000
Smoking	-0.027	0.031	-0.098	0.024	0.060	-0.034
Group Assignment	-0.079	-0.041	-0.088	0.040	0.016	0.003
SF-36 MH	0.316	0.347	0.167	-0.206	-0.050	-0.037
Comorbidities	-0.044	-0.083	0.074	0.094	0.094	-0.036
BMI	-0.070	-0.125	-0.289	0.114	0.115	0.032
age*function	0.773	0.938	0.375	-0.124	-0.046	-0.009

	Smoking	Group Assignment	SF-36 MH	comorbidities	BMI	age*function
WOMAC pain						
WOMAC function						
Age						
Back Pain						
Diabetes						
Respiratory Disease						
Smoking	1.000					
Group Assignment	-0.030	1.000				
SF-36 MH	-0.071	-0.041	1.000			
Comorbidities	-0.007	-0.024	-0.106	1.000		
BMI	0.049	0.027	-0.104	0.038	1.000	
age*function	-0.004	-0.063	0.366	-0.062	-0.203	1.000

Appendix G

VIF with 3-5 year WOMAC pain scores as outcome, with and without interaction term

Variable	**VIF**
Age*function	69.16
Baseline WOMAC Function	61.45
Baseline WOMAC Pain	2.84
Age	8.46
BMI	
≤24.9‡	
25 - 29.9	2.15
30 - 34.9	2.11
>35	1.96
SF-36 MH	1.23
Back Pain	1.10
Gender	1.09
Comorbidities	
*≤ 2**	
≥ 3	1.04
Group Assignment	1.03

Variable	**VIF**
Baseline WOMAC Function	2.94
Baseline WOMAC Pain	2.84
Age	1.16
BMI	
≤24.9‡	
25 - 29.9	2.15
30 - 34.9	2.10
>35	1.96
SF-36 MH	1.22
Back Pain	1.10
Gender	1.08
Comorbidities	
*≤ 2**	
≥ 3	1.03
Group Assignment	1.03

Appendix H

Interactions with 3-5 year WOMAC function score as outcome

Interaction	β	SE	P-value
Comorbidities * SF-36 MH Score (≤ 2 comorbidities = 0)	-0.14	0.17	0.4
WOMAC Pain Score * SF-36 MH Score	0.004	0.003	0.2
BMI * WOMAC Function Score			
≤24.9ǂ			
25 - 29.9	0.041	0.14	0.77
30 - 34.9	0.11	0.16	0.48
>35	-0.04	0.19	0.85
BMI * WOMAC Pain Score			
≤24.9ǂ	0.02	0.14	0.91
25 - 29.9	0.13	0.16	0.40
30 - 34.9	0.05	0.17	0.77
>35			
Gender * WOMAC Pain Score	0.05	0.11	0.63
Gender * WOMAC Function Score	-0.053	0.11	0.62
Age * WOMAC Pain Score	0.005	0.005	0.37
Age * WOMAC Function Score	0.007	0.005	0.21
Age * Gender	0.13	0.21	0.54

ǂ Reference group

Appendix I

Forward and backward stepwise regression for 3-5 year WOMAC function scores

	Forward Stepwise Regression			Backward Stepwise Regression		
Variable	β^+	SE	P-Value	β^+	SE	P-Value
WOMAC function score	0.27	0.06	<0.001	0.27	0.06	<0.001
SF-36 MH score	0.16	0.07	0.18	0.16	0.07	0.02
Age	-0.39	0.11	<0.001	-0.41	0.11	<0.001
Back pain	-6.03	2.0	0.003	-6.19	2.0	0.002

Forward stepwise regression R^2 = 0.16
Backward stepwise regression R^2 = 0.17
$^+$ = Regression Coefficient
Legend: SE= Standard Error

Appendix J

VIF with 3-5 year WOMAC function scores as outcome

Variable	VIF
Baseline WOMAC Function	2.92
Baseline WOMAC Pain	2.84
Age	1.18
Gender	1.09
BMI	
≤24.9‡	
25 - 29.9	2.16
30 - 34.9	2.10
>35	1.97
SF-36 MH	1.23
Back Pain	1.11
Lung Disease	1.03
Comorbidities	
*≤ 2**	
≥ 3	1.04
Group Assignment	1.03

Appendix K

Number (%) of subjects by BMI in different categories of time spent walking for exercise or to work per week

	≤ 24.9 kg/m^2	**25-29.9 kg/m^2**	**30-34.9 kg/m^2**	**≥ 35 kg/m^2**
No time	10 (16.39)	13 (9.42)	26 (23.42)	13 (17.57)
1-59 min	12 (19.67)	39 (28.26)	23 (20.72)	25 (33.78)
1hr – 1hr 59 min	11 (18.03)	27 (19.57)	15 (13.51)	9 (12.16)
2-3 hours	13 (21.31)	25 (18.12)	17 (15.32)	8 (10.81)
4-6 hours	6 (9.84)	19 (13.77)	18 (16.22)	9 (12.16)
≥ 7 hours	9 (14.75)	15 (10.87)	12 (10.81)	10 (13.51)