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Total Knee Replacement

An Evidence-Based Analysis

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Executive Summary

Objective

The aim of this review was to assess the effectiveness, in terms of pain reduction and functional improvement, and costing of total knee replacement (TKR) for people with osteoarthritis for whom less invasive treatments (such as physiotherapy, analgesics, anti-inflammatory drugs, intra-articular steroids, hyaluronic acids, and arthroscopic surgery) have failed.

Clinical Need

Osteoarthritis affects an estimated 10% to 12% of Canadian adults. The therapeutic goals of osteoarthritis treatment are to improve joint mobility and reduce pain. Stepwise treatment options include exercise, weight loss, physiotherapy, analgesics, anti-inflammatory drugs, intra-articular steroids and hyaluronic acids, arthroscopic surgery, and, in severe cases, total joint replacement with follow-up rehabilitation. These treatments are delivered by a range of health care professionals, including physiotherapists, occupational therapists, family physicians, internists, rheumatologists, and orthopedic surgeons. TKR is an end-of-line treatment for patients with severe pain and functional limitations. More women than men undergo knee replacement, and most patients are between 55 and 84 years old.

The Technology

TKR is a surgical procedure in which an artificial joint or prosthesis replaces a damaged knee joint. The primary indication for TKR is pain, followed by functional limitation. Usually, a person's daily activities must be substantially affected by pain and functional limitations for him or her to be considered a candidate for TKR.

There are 3 different types of knee replacement prostheses. Non-constrained prostheses use the patient's ligaments and muscles to provide the stability for the prosthesis. Semi-constrained prostheses provide some stability for the knee and do not rely entirely on the patient's ligaments and muscles to provide the stability. Constrained prostheses are for patients whose ligaments and muscles are not able to provide stability for the knee prosthesis.

The most common risks and complications associated with TKR are deep venous thrombosis, infection, stiffness, loosening, and osteolysis. To prevent deep venous thrombosis, patients are treated with heparin prophylactically and/or given support stockings to wear. Patients are also given antibiotics for 24 hours after surgery to minimize the risk of infection. Stiffness is another associated complication. In most patients, it can be avoided by keeping the knee moving in the days and weeks following surgery.

The National Institutes of Health in the United States concluded that the indications for TKR should include the following: radiological evidence of joint damage, moderate to severe persistent pain that is not adequately relieved by nonsurgical management, and clinically significant functional limitation resulting in diminished quality of life.

Review Strategy

In March 2005, the following databases were searched: Cochrane Library International Agency for Health Technology Assessment (first quarter 2005), Cochrane Database of Systematic Reviews (first quarter 2005), Cochrane Central Register of Controlled Trials (first quarter 2005), MEDLINE (1966 to March

2005), MEDLINE In-Process and Other Non-indexed Citations (1966 to March 14, 2005), and EMBASE (1980 to 2005 week 9). The Medical Advisory Secretariat also searched Medscape on the Internet for recent reports on trials that were unpublished but that were presented at international conferences. In addition, the Web site Current Controlled Trials (www.controlled-trials.com) was searched for ongoing trials investigating TKR or unicompartmental knee replacement.

No studies were identified that compared TKR to an alternative treatment. Several studies have been reported that compare preoperative measurement scores on targeted measures of functioning and pain to postoperative measurement scores in patients undergoing various TKR procedures.

In order for the Medical Advisory Secretariat to measure the effectiveness of TKR and to compare the effectiveness of TKR across studies, effect sizes were calculated in studies that reported the standard deviations of the preoperative and postoperative measurement scores. Percent change was also calculated. For this review, a 20% improvement in outcome score was defined as the minimal clinically important difference.

Summary of Findings

Overall, patients who undergo TKR surgery for osteoarthritis have substantial improvements in terms of reduction of pain and improvement of function. A comparison of the mean effect score and the percent change in 19 studies that reported preoperative and postoperative outcome scores for patients who had TKR showed that the procedure is effective. The 19 studies included patients of various ages and used a variety of prostheses and techniques to implant the device. TKR was effective in all of the studies. The revision rates ranged from 0% to 13% in the studies that reported at least 5 years of follow-up.

As for the factors that predict TKR outcomes, a variety of factors have been evaluated, including obesity, age, gender, prosthesis design, and surgical techniques; however, none of these have been shown to predict outcomes (pain or function) consistently across studies. However, the regression analyses identified accounted for only 12% to 27% of the variance, indicating that over 70% of the variance in the outcomes of TKR is unexplained.

In terms of the timing of TKR surgery, 2 studies found that the severity of osteoarthritis does not predict outcome, but 1 study was found that higher functioning patients had significantly less pain and better function up to 2 years after surgery compared with lower functioning patients. It is important to note that the patients in the low and high function groups were evenly matched on comorbid conditions.

Unicompartmental knee replacement surgery seems to be as effective as TKR surgery for people who meet the indications for it. This is a subset of people who have osteoarthritis of the knee, because for unicompartmental knee replacement to be indicated, only 1 (usually the medial) compartment of the knee can be affected. Patients who undergo this kind of surgery seem to have shorter hospital stays and faster recovery times than do patients who have TKR surgery.

Conclusion

There is substantial evidence to indicate that TKR effectively reduces pain and improves function.

Abbreviations

AHRQ	Agency for Health and Research Quality
BMI	Body mass index
CCAC	Community Care Access Centre
CJRR	Canadian Joint Replacement Registry
HSSK	Hospital for Special Surgery Knee (scale)
HTO	High tibial osteotomy
KSCRS	Knee Society Clinical Rating Scale
NIH	National Institutes of Health
NJOH	New Jersey Orthopaedic Hospital Score
OJRR	Ontario Joint Replacement Registry
RCT	Randomized controlled trial
SF-36	Medical Outcomes Study 36-Item Short-Form Health Survey
TKR	Total knee replacement
UKR	Unicompartmental knee replacement
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Objective

The aim of this review was to assess the effectiveness, in terms of pain reduction and functional improvement, and costing of total knee replacement (TKR) for people with osteoarthritis for whom less invasive treatments (such as physiotherapy, analgesics, anti-inflammatory drugs, intra-articular steroids, hyaluronic acids, and arthroscopic surgery) have failed.

Background

Clinical Need: Target Population and Condition

In 2003, Statistics Canada reported that 16.8% of the Canadian population over the age of 12 has arthritis. (1) Osteoarthritis affects an estimated 10% to 12% of Canadian adults. It results from the deterioration of the cartilage in one or more joints and causes joint damage, pain and stiffness, and disability. About 6% of Canadians aged 35 years and older have osteoarthritis of the knee. Each year, almost 44,000 surgical procedures are done in Ontario for arthritis and related disorders.

The therapeutic goals of osteoarthritis treatment are to improve joint mobility and reduce pain. Stepwise treatment options include exercise, weight loss, physiotherapy, analgesics, anti-inflammatory drugs, intra-articular steroids and hyaluronic acids, arthroscopic surgery and, in severe cases, total joint replacement with follow-up rehabilitation. A range of health care professionals that includes physiotherapists, occupational therapists, family physicians, general internists, rheumatologists, and orthopedic surgeons delivers these modalities.

Canadian Joint Replacement Registry

The Canadian Joint Replacement Registry (CJRR) is a national registry that collects data on hip and knee replacements in Canada. The registry monitors the joint replacement recipients' outcomes. As of September 2003, 63% of the orthopedic surgeons in Canada were participating in the registry. (2) In the CJRR's 2004 annual report, (2) they indicated that the number of TKR surgeries rose by 61.6% between 1994 and 1995 and 2001 and 2002 (15,360 and 24,815, respectively).

More women than men undergo TKR: the age-standardized rates in 2001 to 2002 were 80.4 per 100,000 women and 63.5 per 100,000 men. Compared with other provinces, Ontario has the second highest age-standardized rate of TKR among women (100.8 per 100,000) after Manitoba (107.2 per 100,000). Among men, Ontario had the third highest age-standardized rate of TKR (79.0 per 100,000 men) after Manitoba (83.5 per 100,000) and PEI (80.5 per 100,000). In terms of age, 40% of TKR surgeries were performed in patients aged 65 to 74 years, 8% were performed in patients younger than 55 years, and 3% were for patients older than 85 years. The primary diagnosis leading to TKR is degenerative osteoarthritis (93%). Other diagnoses are inflammatory arthritis (5%), post-traumatic osteoarthritis (2%), and osteonecrosis (when bone dies due to blocked blood supply; 1%).

Ontario Joint Replacement Registry

The Ontario Joint Replacement Registry (OJRR) is a provincial registry, which, similarly to CJRR, collects data on hip and knee replacements in the province. The OJRR data is included in the database for CJRR. The OJRR has been collecting data since 2001. The OJRR has 2 primary objectives: to measure wait times and to document the rates of revisions.

The OJRR's 2004 annual report (3) indicated that 69% of orthopedic surgeons in the province participate in the registry. Surgeons in Toronto have the lowest registry participation rate (56%). OJRR estimates that it is capturing data on about 43% of the knee and hip replacements in the province. One reason why orthopedic surgeons may choose not to participate in the registry is because it takes time for administrative staff to input the patient data into the registry (about 30 minutes per patient) (Personal communication, April 4, 2005).

The 2004 report indicated that 94% of knee replacement surgeries were total knee replacements and 6% were unicompartmental knee replacements (UKR). Total (also known as tricompartmental) knee replacements replace the entire knee, while unicompartmental knee replacements replace only one part of the knee joint. According to an expert consultant, the number of unicompartmental knee replacements is increasing due to improvements in surgical techniques and prosthetic devices. Thus, even though only 6% of the knee replacements in the province are unicompartmental, this report will address unicompartmental knee replacements and report on any new and emerging evidence on the effectiveness of this surgery.

Similar to the CJRR data, more women than men undergo knee replacement and most patients are between 55 and 84 years old. The OJRR 2003 annual report (4) reported the number of knee replacements according to body mass index (BMI). BMI is measure of body fat based on height and weight. If a person has a BMI between 20 and 25 he or she is considered to have a healthy weight; a person with a BMI between 26 and 29 is considered to be overweight; and a person with a BMI greater than 30 is considered to be obese. About 54% of the patients undergoing knee replacement had a BMI of 30 or greater (i.e., they were obese). In total, 84% of patients undergoing knee replacement were overweight or obese (BMI > 25). The 2004 report did not report data according to BMI.

New Technology Being Reviewed: Total Knee Replacement

TKR is a surgical procedure in which an artificial joint or prosthesis replaces a damaged knee joint. The primary indication for TKR is pain, followed by functional ability. Usually, a person's daily activities must be significantly affected by pain and functional limitations for him or her to be considered a candidate for TKR.

Most referrals for pain or functional limitations to orthopedic surgeons come from family physicians (90%); however, some come from rheumatologists (10%). The mean length of hospital stay for TKR is 5 days. Most patients undergo spinal anesthesia. The surgical procedure typically lasts 2 hours. After the patient is discharged from hospital, rehabilitation is prescribed, either on an inpatient basis at a rehabilitation hospital or through outpatient care with a Community Care Access Centre (CCAC). Patients undergo short-term deep vein thrombosis prevention treatment after joint replacement (for 1 to 6 weeks). Patients are also given antibiotics for 24 hours immediately following the surgery to prevent infection. Follow-up usually occurs at 6 weeks, 12 weeks, 1 year, and then every 2 years.

The type of prosthesis offered depends upon the patient's age, weight, gender, anatomy, activity level, medical history, and general health. The device's performance record and the surgeon's experience with the device also influence the decision. There are 5-10 manufacturers licensed to distribute knee replacement components in Canada.

There are 3 basic types of knee replacement prostheses:

- Non-constrained:
  - This is the most common type of knee replacement prosthesis.
  - The components of the prosthesis inserted into the knee are not linked to each other.
  - The patient's ligaments and muscles provide the stability for the prosthesis.

- Semi-constrained:
  - This prosthesis provides some stability for the knee and does not rely entirely on the patient's ligaments and muscles to provide the stability.
  - This type of prosthesis is used if the orthopedic surgeon needs to remove all the ligaments of the inner knee.

- Constrained (also called hinged):
  - The components of the prosthesis are linked or "hinged" together.
  - This prosthesis is used when a patient's ligaments and muscles are not able to provide stability for the knee prosthesis.
  - This prosthesis is more common in patients undergoing revision surgery.
  - This type of device does not usually last as long as the other types of prostheses.

There are 3 options for holding the knee replacement prosthesis in place: the prosthesis can be cemented, non-cemented or attached using a hybrid fixation procedure. The cemented procedure fixes the prosthesis to the bones with polymethylmethacrylate. The cement allows the prosthesis to fit perfectly to the bone, even if there are bone irregularities. A cemented knee replacement stabilizes rapidly, so patients can walk (i.e., bear weight on the joint) immediately following surgery. The disadvantage is that if the cement loosens, then bone may be ground away by movement of the joint, making subsequent revisions difficult.

The non-cemented procedure uses a prosthesis with a rough porous surface that is designed to let bone grow into it, thus eliminating the need for cement. The prosthesis is fitted precisely next to the bone and fixed into place with metal pegs and screws while the bone grows and fixes to the knee replacement prosthesis. As would be expected, there is a longer recovery time to walking (i.e., weight-bearing) compared to using cemented prostheses. The advantage is that if the prosthesis does loosen over time, then less bone loss occurs due to the lack of the irritant cement.

Hybrid fixation is a combination of cemented and non-cemented procedures. The femur is cemented, while the tibia is not. Hybrid fixation and non-cemented procedures are relatively new procedures, and the long-term outcomes of patients undergoing these types of fixation technique are unknown. At this time, most knee replacement surgeries use the cemented procedure. The OJRR annual report from 2004 reported that 80% of the knee replacements were cemented, 13% were hybrids, and 7% were non-cemented. (3)

Risks and Complications Associated With Knee Replacement

The most common risks and complications associated with knee replacement are deep venous thrombosis (DVT), infection, stiffness, loosening, and osteolysis (the softening and loss of bone). DVT is the formation of blood clots in large veins, usually in the legs or pelvis. It is more likely to occur after surgery involving the lower body compared to other surgeries. To prevent DVT, patients are treated with heparin prophylactically and/or given support stockings to wear. Patients are also given antibiotics for 24 hours after surgery to minimize the risk of infection. Stiffness is another associated complication. In most patients, it can be avoided by keeping the knee moving in the days and weeks following surgery.

In terms of revisions, one of the primary reasons why joint replacements fail is due to loosening of the prosthesis from the bone. As technology continues to improve, improvements will be made to the fixation

methods to prevent loosening. Another reason for revision is osteolysis, which is a breakdown of bone that can occur if tiny particles of worn-out plastic or cement migrate into the bone and damage it.

Unicompartmental Knee Replacement

UKR differs from TKR in that only a portion of the knee is replaced. UKR was developed at the same time as TKR; however, the procedure has not been as widely accepted by the orthopedic community owing to early reports of poor results associated with the procedure. These early studies were misleading, because further review of these studies indicated that the poor results associated with UKR might have been due to patient selection, the type of prosthesis used, and surgical technique. Identification and correction of pitfalls in the surgical technique, plus the development of better implant designs, have renewed enthusiasm for UKR in certain selected patients. In the past 5 to 10 years, UKR has become more popular. (5)

UKR is done under a spinal or general anesthetic. The surgery takes about 1.5 hours. The rough edges of the end of the femur and top of the tibia are cut flat, cleaned, and then the device is cemented in place.

Indications for Knee Replacement

According to the Canadian Orthopaedic Association, (http://www.coa-aco.org/library_NEW/Minimally_Invasive_Unicompa.asp) the indications for UKR are as follows:

- Significant pain related to medial compartment osteoarthritis (especially upon weight bearing).
- Mostly medial pain, with no significant anterior or lateral pain.
- Varus deformity not larger than 15°.
- Fixed flexion deformity not larger than 15°.
- Flexion greater than 120°.
- Correctable varus deformity.
- Intact lateral compartment.
- Intact anterior and posterior cruciate ligaments.
- In the absence of anterior knee pain, the status of the patellofemoral joint is irrelevant, unless there is severe degeneration.
- X-ray showing narrowing at predominately one side of the joint.
- Failure to respond to non-operative care or operative efforts at cartilage treatment (repair, replacement, or regeneration of articular cartilage).

In December 2003, the National Institutes of Health (NIH) (6) in the United States published a consensus statement on TKR (based on the Agency Healthcare Research and Quality's Technology Assessment, (7) which will be discussed in detail later in this report) that concluded the indications for TKR should include these:

- Radiologic evidence of joint damage
- Moderate to severe persistent pain that is not adequately relieved by nonsurgical management
- Clinically significant functional limitation resulting in diminished quality of life

A review of the evidence for knee replacement for osteoarthritis by Dieppe et al. (8) from 1999 indicated there were no evidence-based indications for TKR in patients with osteoarthritis. Dieppe et al. identified 3 studies that reported indications for TKR based on consensus. They reported that daily pain, radiological evidence of loss of joint space, severity of functional impairment, and high patient motivation to have the procedure were indications for TKR. Active infection was an absolute contraindication, and young age (<

60 years), poor compliance, regional pain disorders, and unrealistic expectations were relative contraindications.

Wait Times for Knee Replacement in Ontario

There are 3 periods of waiting for knee replacement: the time from initial referral to orthopedic surgeon to the consultation, then the time from the consultation to the decision regarding joint replacement, and finally the time between the decision and joint replacement surgery. It is important to note that the decision to have the joint replacement is made at the first consultation in 82% of patients—thus there are usually only 2 wait times, the time between referral and consultation and the time between consultation and surgery. Wait times vary considerably, but can range from a few days to more than 1 year (Personal communication, April 4, 2005). According to the OJRR's 2004 annual report, the median wait time from consultation to surgery was 125 days (about 4 months) in 2003/2004. (3)

While in Ontario the waiting list for patients undergoing joint replacement is done on a first-come, first-served basis, the OJRR 2004 annual report indicates that people with more severe pain appear to undergo surgery sooner than those reporting less severe pain. The OJRR also established that people who depend on others to help them with their activities of daily living because of their joint pain or dysfunction, receive joint replacement surgery sooner than people who are not dependent on others.

The purpose of this health technology policy assessment is to determine the effectiveness of knee replacement, not to specifically address the concerns with wait times. The Ministry of Health and Long-Term Care has an ongoing initiative to address waiting times for knee replacement in Ontario (Health Results Team http://www.health.gov.on.ca/transformation/hresults.html).

Existing Treatments Other Than Technology Being Reviewed

TKR is an end-of-line treatment for patients with severe, unmanageable knee pain. It has no equivalent alternatives.

A possible alternative treatment to UKR is high tibial osteotomy (HTO). High tibial osteotomy is an operation where the tibial bone is cut at its upper end and repositioned. HTO works best in patients with isolated medial compartment arthritis, particularly if they are younger than 50 years old and have at least 120 degrees of knee flexion. UKR has similar indications to HTO but is usually reserved for patients aged over 60 years (Personal communication, April 25, 2005).

In 2001, Stukenborg-Colsman et al. (9) published a randomized controlled trial (RCT) comparing HTO (n = 32) to UKR (n = 28). The patients were assessed about 2.5 years after surgery (range, 1.6–5 years), 4.5 years after surgery (range, 3.6–7 years), and 7.5 years after surgery (range, 6.6–10 years).

The 2 groups were comparable at baseline in terms of age and preoperative Knee Society Clinical Rating Scale (KSCRS) (overall and functional); however, 78% of the patients in the UKR group were female compared to only 40% in the HTO arm. Also, patients in the UKR group had more severe arthritis preoperatively than did the patients in the HTO group. About 31% of the patients in the UKR group were considered to have severe arthritis preoperatively, compared to 25% in the HTO group. Fifty-five percent of the patients in the HTO group had stage I arthritis preoperatively compared to 38% of the patients in the UKR group. Stukenborg-Colsman et al. reported that patients were computer-randomized.

Two weeks after surgery, the overall KSCRS score for the patients in the HTO group was 61/100 compared with 39/100 for the patients in the UKR group. The KSCRS is described in detail later in the review; however, it is important to note that a score over 85 are excellent; 70 to 84 is good; 60 to 69 is

fair; and less than 60 is poor. Thus, after 2 weeks, the scores for patients who had HTO were fair, and those for patients who had UKR were poor. However, as time progressed, people in both groups continued to improve. At a mean of 2.5 years follow-up, the KSCRS overall scores were 77 for the people who had had HTO and 81 for those who had had UKR. The function score was 70 for both groups at 2.5 years. After 7.5 years follow-up, there was a slight decrease in the scores in the UKR group overall (75) and for function (59); however, the scores for HTO remained the same overall and for function. There were no significant differences between HTO and UKR in terms of KSCRS scores at any follow-up time.

Ten patients in the HTO group required revision surgery to TKR compared with 6 patients in the UKR group. More patients undergoing HTO also had postoperative complications (n = 9, 28% complication rate) compared to the patients in the UKR group (n = 2, 7% complication rate). Stukenborg-Colsman et al. did not report any details regarding the power of the study to detect significant differences between groups. In addition, the 2 groups were not comparable on severity of arthritis; the UKR group had more patients with severe disease. Nonetheless, the outcomes for both groups were not significantly different in terms of KSCRS scores (even though patients undergoing UKR had more severe osteoarthritis), and there were substantially more complications in the HTO group.

Preliminary results of an RCT by Borjesson et al. (10) comparing HTO to UKR were published in 2005. This preliminary report included outcomes on 40 patients up to 5 years after surgery. (The completed study will include 100 patients with 5 years of follow-up data.) The patients were comparable at baseline in terms of age, weight, gender, and stage of arthritis. The authors reported no significant differences between the groups on range of motion, British Orthopaedic Association scores, or physical activity. Patients in both groups improved significantly after surgery. Borjesson et al. did not report any data on complications

Thus, based on the results of two RCTs comparing UKR to HTO, there does not seem to be a difference in terms of outcomes based on standardized scores. It is important to note, however, that neither of the RCTs were likely sufficiently powered to detect significant differences between groups should those differences have existed. Furthermore, HTO does seem to have a higher complication profile than UKR, but this conclusion needs to be interpreted cautiously because it is based on the results of one small RCT.

Measuring Effectiveness of Knee Replacement

Several scales have been used to measure the effectiveness of TKR. The most commonly used scales are the KSCRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). The SF-36 is the only generic scale identified to measure outcomes of knee replacement, the other scales are specific to knee replacement or osteoarthritis. Both the WOMAC and SF-36 require licences to use them. These licences are free for clinical and educational use (both are available online at www.womac.org and www.sf-36.com). (11) Both the WOMAC and the SF-36 scales are self-reported. A clinician completes the KSCRS. Table 1 shows a comparison of scales used to measure the effectiveness of knee replacement.

The KSCRS was derived from the Hospital for Special Surgery knee scale (HSSK). The HSSK score was developed in 1974 when knee replacement surgery was in its early stages and expectations were not as high as they are now. (12) The main difference between the 2 scores is that the KSCRS separates the scores for pain and function, while the HSSK combined the pain and function scores to come up with an overall score. The proposed advantage of the KSCRS is that the knee score would be independent of function and, therefore, not subject to deterioration due to increasing age or comorbid conditions. (11) The scale of outcome for the KSCRS, HSSK, and the New Jersey Orthopaedic Hospital (NJOH) score was the same: scores greater than 85 were excellent; between 70 and 84, good; between 60 and 69, fair; and anything less than 60 was poor.

Lingard et al. (13) conducted a study comparing the validity of the KSCRS to the WOMAC and SF-36. When the preoperative and 12-month postoperative scores were compared across 697 patients who had completed all 3 assessments, Lingard et al. found varying levels of correlation between the scales. In terms of preoperative pain scores, the lowest correlation was between the KSCRS and SF-36, and the highest correlation was between the WOMAC and SF-36. For postoperative pain scores, the correlation between the KSCRS and SF-36 was the lowest, and the correlation between the KSCRS and WOMAC was the highest. For preoperative function, the correlation between the KSCRS and WOMAC was the lowest, and the correlation between the KSCRS and SF-36 was the highest. The same trend was observed in the postoperative function. Thus, all 3 scales seem to have some correlation with one another; however, Lingard et al. concluded that the WOMAC and SF-36 should be used instead of the KSCRS because the WOMAC and SF-36 are easier to administer (self-reported) and there is less chance of observer bias than with the KSCRS.

Table 1: Comparison of Outcome Measurement Scales in Knee Replacement Studies

Scale	Generic or specific to OA*	Scores					
		Pain	Function	Range of Motion	Stability	Other	Overall
Hospital Special Surgery Knee Score (HSSK), 1974	Specific	30 points	22 points	18 points	10 points	10 points (strength) 10 points (deformity)	100 points†
Knee Society Clinical Rating Scale (KSCRS), 1989	Specific	50 points	100 points (walking 50, stair climbing 50)	25 points	25 points	—	100 points clinical (pain + ROM* + stability) 100 points functional
New Jersey Orthopaedic Hospital Score (NJOH), 1982	Specific	30 points	25 points	15 points	10 points	12 points (deformity) 8 points (strength)	100 points
Oxford Hip and Knee Score, 1998	Specific	*5 points each:* • Pain • Difficulty with washing and drying self • Difficulty getting into car/public transport • Walking duration • Pain on standing • Limp • Ability to kneel • Night pain • Interference with work • Giving way • Ability to do shopping • Ability to descend stairs					60 points
Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), 1992	Generic	*8 health dimensions*: • Physical function • Role limitation (physical) • Bodily pain • Mental health • Emotional role function • Social functioning • Vitality • General health perception					100 points
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), 1988	Specific	Pain – Walking Pain – Stair climbing Pain – Nocturnal Pain – Rest Pain – Weightbearing	• Descending stairs • Ascending stairs • Rising from sitting • Standing • Bending to the floor • Walking on flat • Getting in/out of a car • Going shopping • Putting on socks • Rising from bed • Taking off socks • Lying in bed • Getting in/out of bath • Sitting • Getting on/off toilet • Heavy domestic duties • Light domestic duties	—	—	• Morning Stiffness • Stiffness occurring during the day	96 points 5-point Likert scale

*OA indicates osteoarthritis; ROM, range of motion.
†Subtractions are made for walking aids, extension lag, and varus deformity.

Literature Review on Effectiveness

Objective

To assess the effectiveness, in terms of pain reduction and functionality, and costing of TKR for people for whom less invasive treatments have been unsuccessful.

Questions Asked

- Is TKR effective in reducing pain and improving function?
- What are the factors related to outcomes for TKR?
- Does the timing of TKR (based on severity) affect outcomes?
- Is UKR effective and safe, in terms of revision and complication rates, compared to TKR?

Methods

Outcomes of interest

- Preoperative and postoperative scores for pain and/or functionality
- Reported patient characteristics as they apply to TKR outcomes

Inclusion Criteria

Studies were included in the review of the effectiveness of TKR if they met each of the following criteria:

- Systematic reviews, RCTs, non-RCTs, case series, or retrospective studies published since 2003.
- At least 80% of the patients in the studies were diagnosed with osteoarthritis.
- Reported at least one outcome of interest.
- Included $\geq$100 TKR procedures.
- English language.
- Abstracts or full reports.

Studies were included in the review of the factors related to the outcomes of TKR and the timing of TKR if they met each of the following criteria:

- Systematic reviews, RCTs, non-RCTs, case series, or retrospective studies published since 1995.
- At least 80% of the patients in the studies were diagnosed with osteoarthritis.
- For studies measuring if obesity is a factor, BMI must be used to determine obesity.
- Reported at least one outcome of interest.
- English language.
- Abstracts or full reports.

Studies were included in the review of UKR if they met each of the following criteria:

- Systematic reviews, RCTs, non-RCTs, case series, or retrospective studies published since 1995.
- At least 80% of the patients in the studies were diagnosed with osteoarthritis.
- Reported at least one outcome of interest.
- English language.
- Abstracts or full reports.

Exclusion Criteria

Studies were excluded from this report if any of the following applied:

- Duplicate publications (superseded by another publication by the same investigator group, with the same objective and data)
- Non-systematic reviews, letters, editorials, or case reports
- Animal or in-vitro studies

Databases and Search Strategy

- Search date: March 14, 2005
- Databases: Cochrane Library International Agency for Health Technology Assessment (first quarter 2005), Cochrane Database of Systematic Reviews (first quarter 2005), Cochrane Central Register of Controlled Trials (first quarter 2005), MEDLINE (1966 to March 2005), MEDLINE In-Process and Other Non-indexed Citations (1966 to March 14, 2005), and EMBASE (1980 to 2005 week 9)
- Search terms: total knee replacement, total knee arthroplasty, unicompartmental knee arthroplasty.

The Medical Advisory Secretariat also conducted Internet searches of Medscape for recent reports on trials that were unpublished but that were presented at international conferences. In addition, the Web site, Current Controlled Trials (www.controlled-trials.com) was searched for ongoing trials on TKR or UKR.

The detailed literature search strategy is listed in Appendix 1.

Integrating the Evidence and Establishing Clinical Significance

No study was identified that compared TKR to an alternative treatment. In fact, no study was identified whose specific purpose was to establish if TKR was effective at reducing pain and increasing functional ability. Several studies have been reported comparing preoperative measurement scores (WOMAC, KSCRS, HSSK, SF-36) to postoperative measurement scores in patients undergoing various knee replacement procedures. However, because these studies were not designed to measure the effectiveness of TKR, they typically did not report the statistical significance of the comparison between preoperative and postoperative measurement scores. For the Medical Advisory Secretariat to measure the effectiveness of TKR and to compare the effectiveness of TKR across studies, effect sizes were calculated in studies that reported the standard deviation of the preoperative and postoperative measurement scores. The effect size is defined as "the degree to which the phenomenon is present in the population." (14) It is a way of quantifying the difference between preoperative and postoperative scores.

For the purpose of this report, effect size was calculated as follows:

$$\frac{\text{Mean of the postoperative measurement score} - \text{Mean of the preoperative measurement score}}{\sqrt{(\text{standard deviation}_{(\text{postop})}^2 + \text{standard deviation}_{(\text{preop})}^2)/2}}$$

Effect size can be converted into statements about the overlap between 2 samples in terms of a comparison of percentiles. Assuming there is normal distribution, an effect size is equivalent to a Z score. For instance, an effect size of 0.8 indicates that the average postoperative score is greater than 80% of the preoperative scores. The greater the effect size is, the greater the difference between preoperative and postoperative scores. According to Cohen, (14) an effect size of 0.2 represents a small difference, an effect size of 0.5 represents a medium difference, and an effect size greater than 0.8 represents a large difference between preoperative and postoperative scores.

The studies were stratified by years of follow-up (less than 1 year, 1 year, 2–5 years, and more than 5 years), and measurement score. The pooled mean age, pooled proportion of female patients, pooled weight (in kilograms and BMI), and pooled proportion of patients with osteoarthritis were calculated.

The following was used for the pooling calculation:

$$\frac{\Sigma\ (N * \text{variable (age, weight, etc.)})}{\Sigma\ N}$$

It is important to establish the minimally clinically important difference, because statistical significance does not necessarily equate to clinical significance. The minimally clinically important difference is "the smallest difference in score (i.e., the effect that patients perceive as beneficial and which would then mandate, in the absence of troublesome side effects and excessive costs, a change in the patient's management." (15) The study by Angst et al. (15) tried to establish the minimally clinically important difference in patients after knee replacement. Using WOMAC, they found that an improvement of about 20% in scores reflected a "slightly better" improvement in outcome. They found an 18% difference in pain, 22% difference in stiffness, a 17% difference in function, and a 18% overall change was equivalent to a "slightly better" improvement in outcomes. They reported that this was consistent with other studies measuring minimally clinically important differences for patients with osteoarthritis and other conditions (chronic respiratory disease and chronic heart failure). (16;17) This 20% difference was also reported in a study measuring the minimally clinically important difference in patients with rheumatoid arthritis using SF-36. (18)

Jensen et al. (19) reanalyzed the results of 2 RCTs (one for TKR and another for laparotomy) to try to determine a meaningful change in pain from the patient's perspective consistent across the studies. They found that a 33% reduction in pain (using a visual analog scale) was meaningful from a patient's perspective.

Based on the aforementioned studies and for the purpose of this review, a 20% improvement in overall outcome or function score was defined as the minimal clinically important difference. Pain scores must have decreased by at least 33% after surgery to be considered meaningful or clinical important.

The percent change was measured using the following formula:

$$\%\ \text{change} = 100 * ((\text{postoperative score} - \text{preoperative score})/\text{preoperative score})$$

Results of Literature Review

For this review, an *a priori* decision was made not to look at the types of devices and compare the differences between the devices for surgical technique, fixation technique, or in variation of the design of the prosthesis. The primary purpose of this systematic review was to establish if knee replacement is effective at decreasing pain and improving function. As the systematic review was being conducted, if it was evident that the differences between surgical technique, fixation technique, or in variation of the design of the prosthesis were substantially affecting the effectiveness of the knee replacement, then the differences was investigated.

Summary of Existing Health Technology Assessments

In 2003, the Agency for Healthcare Research and Quality (AHRQ) published a health technology assessment on TKR. (7) They included 62 studies, limited to those with at least 100 TKR procedures and reported preoperative and postoperative data for patients using at least one of the following standard

functional measures: the KSCRS, HSSK, WOMAC, or SF-36. They included only studies on patients who were having TKR; they did not include studies of patients undergoing UKR.

Among the 62 studies, the weighted mean age of the patients was 69.1 years. Almost 65% of the patients were women, 87% had osteoarthritis, and about 37% of the patients were obese (BMI > 30). Most of the studies used the KSCRS as their outcome measure. AHRQ hypothesized that the KSCRS measure was used most frequently because it is one of the oldest standard measures and is specific to knee surgery (unlike SF-36).

The authors stratified the outcomes of the studies by number of years of follow-up and outcome measure (0–2 years follow-up, 2–5 years follow-up, more than 5 years follow-up). They reported the mean effect size (defined as the number of standard deviations of change) for each stratum. They found that across length of follow-up and outcome measures, functional scores after TKR were higher than they were before surgery. The mean effect sizes for each stratum were greater than 1 standard deviation. An effect size greater than 1 standard deviation is considered to be large. The mean effect sizes were lower for the SF-36 measure; however, the authors suggested that this was expected owing to the more generic nature of SF-36 compared with the other functional measures.

They reported factors related to outcomes of TKR. It is important to note that these are not indications for TKR. Indications for TKR are the characteristics that warrant TKR, while the factors related to outcomes refer to whether outcomes vary according to a patient's clinical or demographic characteristics. The most frequently reported factors related to outcome were age, body weight, and type of arthritis. They found that neither age nor obesity was correlated with TKR outcomes (in studies ranging from less than 1 year to more than 5 years of follow-up). One of the questions that they aimed to answer was "[w]hat are the indications for total knee replacement?" Unfortunately, they did not answer this question.

After the publication of the AHRQ's assessment, the National Institutes of Health (NIH) (6) released a consensus statement on TKR based on the AHRQ's results and expert opinion. They concluded that after TKR "[t]here appears to be rapid and substantial improvement in the patient's pain, functional status, and overall health-related quality of life in about 90 percent of patients."

Ethgen et al. (20) published a systematic review in 2004 that reviewed quality of life in patients who had undergone knee or hip replacement. Between 1980 and 2003, they identified 74 studies that met their inclusion criteria: 32 investigating hip and knee replacement, 16 on knee replacement only, and 26 on hip replacement only. Ethgen et al. reported on a variety of outcomes, including the effect of age and gender; osteoarthritis versus rheumatoid arthritis, and cost-effectiveness. They found varying reports for the effect of age on total knee or hip replacement, with little consistency across studies in which patients (older versus younger) reported improvement in terms of pain and function. They reported that 5 studies measured the effect of gender on knee or hip replacement; in 3 studies, the replacement surgeries seemed to have a greater improvement among men on pain and function; in 2, there was no difference between men and women on pain and function. Four studies compared outcomes in patients who had osteoarthritis versus patients with rheumatoid arthritis; in all 4, even though all patients improved, those with osteoarthritis improved significantly more than the patients with rheumatoid arthritis.

A limitation of the systematic review by Ethgen et al. (20) is that they did not critique the quality of the studies the included. While they reported several inconsistencies in the literature, it is difficult to assess whether this variability truly exists in the population of patients undergoing knee and hip replacements, or if it was due to differences in study quality.

Summary of Medical Advisory Secretariat Review

No RCT was identified that compared TKR to an alternative treatment (e.g., drug therapy, physical therapy, arthroscopy, or debridement). It is unlikely that there ever will be such an RCT, because TKR is a commonly accepted procedure, and ethically it would be difficult to randomize patients to not receive TKR. Accordingly, the highest quality evidence available to assess the effectiveness of TKR is that given by observational studies. Table 2 lists the studies that met the inclusion criteria for this review.

Table 2: Quality of Evidence of Included Studies

Study Design	Level of Evidence	Number of Eligible Studies
Non-RCT with contemporaneous controls*	3a†	19
Non-RCT with contemporaneous controls	3a	10
Case series (single site)	4c	2
Non-RCT with contemporaneous controls	3a	1 + 1 update
Case series (single site)	4c	1
Retrospective review, modeling	4d	1
RCT	2	1
Non-RCT with contemporaneous controls	3a	2
Retrospective review, modeling	4d	1

*RCT refers to randomized controlled trial.
†Studies included for this question were not designed to measure the effectiveness of TKR. The studies were designed to measure other outcomes; however, all of these studies reported preoperative and postoperative scores for the patients, thus they were categorized as level 3a studies.

Effectiveness of Total Knee Replacement

No studies were found since the ARHQ review was published that has compared TKR to an alternative treatment. Several studies have been reported that compared preoperative measurement scores (WOMAC, KSCRS, HSSK, SF-36) to postoperative measurement scores in patients undergoing various TKR procedures. The objective in these studies was not to report the effectiveness of TKR; nonetheless, they were included because they did report a measure of effectiveness.

Table 3 lists a comparison of the quality of these studies. All used a standardized outcome measure to compare preoperative and postoperative outcomes. Most reported specific inclusion and exclusion criteria. The most infrequently reported item was a justification of the sample size recruited. It is important to note that these studies vary from observational studies to RCTs, and the studies that did not report a justification for the sample size were not limited to one type of study design. For length of follow-up, less than 1 year was considered inadequate. To measure overall quality, 0 to 2 checkmarks were considered poor quality, 3 to 4 were considered moderate quality, and 5 were considered high quality. Most of the studies were moderate quality. Only 2 were high quality (i.e., addressing all quality indicators), both of which were RCTs. Overall, the quality of the 19 studies is moderate.

Table 3: Quality of Evidence for Preoperative and Postoperative Studies

Study	Design*	Sample Size Justification	Inclusion/ Exclusion Criteria	Standardized Outcome Measure	≥ 1 Year Follow-Up	No Serious Limitations	Overall Quality
Bankes, 2003 (21)	Retrospective review	×	✓	✓	✓	×	Moderate
Brander, 2003 (22)	Prospective case series	×	✓	✓	✓	×	Moderate
Bozic, 2005 (23)	Retrospective review	✓	×	✓	✓	×	Moderate
Fitzgerald, 2004 (24)	Prospective case series	×	✓	✓	✓	×	Moderate
Goldberg, 2004 (25)	Prospective case series	×	✓	✓	✓	✓	Moderate
Hassaballa, 2003 (26)	Prospective case series	×	×	✓	✓	✓	Moderate
Jones, 2003 (27)	Prospective case series	×	✓	✓	×	✓	Moderate
Joshi, 2003 (28)	Prospective case series	×	×	✓	✓	×	Poor
Kim, 2004 (29)	Prospective case series	×	×	✓	✓	✓	Moderate
March, 2004 (30)	Prospective case series	×	✓	✓	✓	×	Moderate
Meding, 2003 (31)	Non-RCT with controls	✓	✓	✓	✓	×	Moderate
Miner, 2003 (32)	Prospective case series	×	✓	✓	✓	✓	Moderate
Pagnano, 2004 (33)	RCT	✓	✓	✓	✓	✓	High
Pynsent, 2005 (34)	Prospective case series	×	✓	✓	✓	×	Moderate
Ritter, 2003 (35)	Retrospective review	×	×	✓	✓	×	Poor
Sansone, 2004 (36)	Prospective case series	×	×	✓	✓	✓	Moderate
Shih, 2004 (37)	Retrospective review	×	✓	✓	✓	×	Moderate
Sorrells, 2004 (38)	Prospective case series	×	×	✓	✓	✓	Moderate
Waters, 2003 (39)	RCT	✓	✓	✓	✓	✓	High

*RCT indicates randomized controlled trial.

Various demographic characteristics were reported within each of the studies; however, the data reported was inconsistent across the studies. To try to compare outcomes across these studies, effect sizes were calculated. Effect size was defined according to the number of standard deviations of change.

Table 4 on the next page shows the characteristics of the studies identified. In this table, the studies have been stratified according to length of follow-up (less than 6 months, 1 year, 2–5 years, and more than 5 years). For the studies that reported weight, some reported weight in kilograms, others reported BMI alone, and others reported weight and BMI. The most heterogeneous measure across the studies was the type of measurement score used (WOMAC, KSCRS, HSSK, SF-36). The overall Knee Society Clinical Rating System was the most frequently reported outcome. At the bottom of Table 4, the pooled means are reported for age, proportion of females in the studies, proportion of patients with osteoarthritis, and pooled mean weight and BMI.

Table 4: Characteristics of Studies Reporting Preoperative and Postoperative Standardized Scores

Study	Length of Follow-up	N/No. Knees*	Female, %	Age, Mean (SD or Range)	Weight†	Osteoarthritis, %	Outcome Measure†
Less than 1 year follow-up							
Jones, 2003 (27)	6 months	276/276	59	69 (9)	BMI: 31.6 (SD, 5.9)	94	WOMAC
1 year follow-up							
Pynsent, 2005 (34)	1 year	1739/1739	63	70 (18–94)	NR	91	Oxford
Fitzgerald, 2004 (24)	1 year	131/254	61	69 (10)	BMI: 28.6 (SD, 4.2)	100	SF-36
March,2004 (30)	1 year	153/209	51	69 (50–87)	NR	100	WOMAC
Pagnano, 2004 (33)	1 year	240/240	70	67 (41–80)	91 kg (53–126)	100	KSCRS
Sorrells, 2004 (38)	1 year	282/371	63	68 (29–88)	80 kg (47–127) BMI: 28.3	85	NJOH
Brander, 2003 (22)	1 year	116/149	55	66 (36–85)	BMI: 30.4 (20.5–56.4)	95	KSCRS
Hassaballa, 2003 (26)	1 year	106/113	NR	72 (NR)	NR	100	Oxford
Miner, 2003 (32)	1 year	684/684	59	70 (38–90)	BMI: 29.5 (SD, 5.7)	100	WOMAC
2-5 years follow-up							
Hassaballa, 2003 (26)	2 years	106/113	NR	72 (NR)	NR	100	Oxford
Meding, 2003 (31)	4.3 years (diabetics)	291/329	52	70 (43–84)	NR	94	KSCRS
	4.8 years (non-diabetics)	3228/4891	60	70 (49–88)	NR	91	KSCRS
Ritter, 2003 (35)	3 years	3998/6200	59	70 (NR)	NR	95	KSCRS
5 or more years follow-up							
Bozic, 2005 (23)	5.8 years	248/287	62	66 (10)	84.7 kg/167 cm BMI: 30.4	87	HSSK
Goldberg, 2004 (25)	> 14 years	99/124	56	62 (32–74)	NR	100	KSCRS
Kim, 2004 (29)	6.4 years	190/380	94	64 (47–76)	NR	85	KSCRS
Sansone, 2004 (36)	6.3 years	102/110	53	72 (50–83)	73 kg/166 cm BMI: 26.5	95	KSCRS
Shih, 2004 (37)	8.5 years	187/235	89	65 (56–78)	66 kg/152 cm BMI: 28.6	100	KSCRS
Bankes, 2003 (21)	6.5 years	194/198	63	69 (48–88)	NR	80	KSCRS
Joshi, 2003 (28)	7.9 years	90/110	69	84 (80–92)	NR	100	KSCRS
Ritter, 2003 (35)	5, 7, 10, 12, 15 years	3998/6200	59	70 (NR)	NR	95	KSCRS
Waters, 2003 (39)	5.3 years	390/474	60	69 (35–89)	78 kg	85	KSCRS
Pooled means			61	70	80 kg BMI: 29.6	93	—

*N/No. Knees: This column reports the total number of participants in a study (N), then the number of knees that were included in the study (in some studies patients with bilateral TKR were included).
† BMI indicates body mass index; HSSK, Hospital for Special Surgery knee scale; KSCRS, Knee Society Clinical Rating Scale; NJOH, New Jersey Orthopaedic Hospital score; Oxford, Oxford Knee Rating Scale; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Mean Effect Size

Eight studies (22;24;26;27;30;31;33;38) reported preoperative and postoperative pain scores for pain. Interestingly, the studies that reported pain measurements also reported the shortest follow-up times compared with the studies that reported function or overall measurements. The KSCRS, WOMAC, SF-36, Oxford hip and knee scale, and the New Jersey Osteoarthritis Hospital (NJOH) score were reported in the 8 studies. Only 3 studies (22;24;27) reported standard deviations around the mean preoperative and postoperative scores, which means that effect sizes could only be calculated for these studies. Even though there were a variety of different pain measurements reported, the effect size was greater than 1.0 in all 3 studies, indicating a large decrease in pain after total knee surgery. In Figure 1, the mean effect sizes for the studies are displayed. Figure 1 highlights 0.8 because any effect size greater than 0.8 indicates there is a large effect between the preoperative and postoperative scores.

Function was a more frequently reported outcome than pain in the studies that reported preoperative and postoperative scores for TKR. Thirteen studies (21;22;24;25;27;28;30-33;36-38) reported function as an outcome measure. Various measures of function were reported, including the WOMAC, KSCRS, SF-36, and NJOH score (Table 5). For the 7 studies (22;24;27;28;32;36;37) that included standard deviations for the preoperative and postoperative function scores, the mean effect size for function ranged from 0.47 to 3.86. (Figure 2) The highest and lowest mean effect sizes were reported using the KSCRS as the measurement scale. Six of the 7 studies measuring function reported effect sizes greater than 0.8, which indicates a large effect. The study that reported an effect size less than 0.8 was done by Joshi et al. (28) and investigated TKR in patients aged older than 80 years using the KSCRS. Their study had an effect size of 0.47 for function; however, the overall effect size was 2.69. Unfortunately, Joshi et al. did not report pain outcomes separately, but the large overall effect size and the smaller function effect size would suggest that there was a substantial improvement in pain.

Thirteen studies (21-23;25;28;30;31;34-37;39) were identified that reported preoperative and postoperative overall measurement scores (KSCRS, WOMAC, HSSK, Oxford hip and knee score). Of the 7 studies that reported standard deviations for the preoperative and postoperative scores, all of the studies reported mean effect sizes much larger than 0.8. The range of mean effect size was between 1.94 and 4.66 (Figure 3).

It is important to interpret these findings cautiously, because none of these studies were designed to measure the effectiveness of TKR specifically.

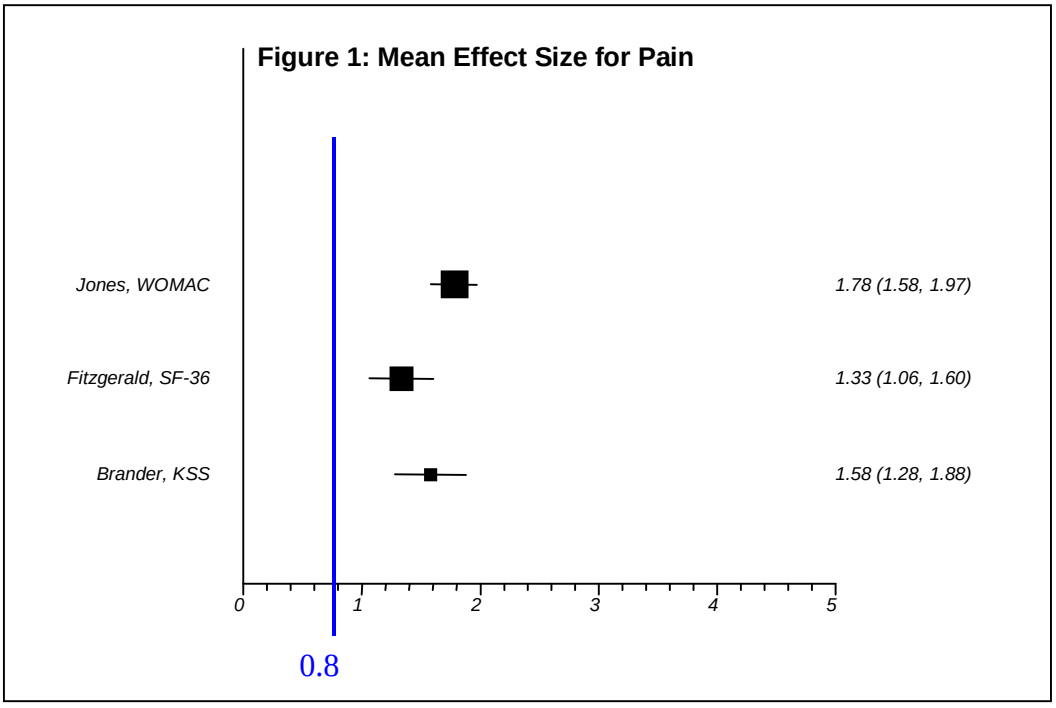


Figure 1: Mean Effect Size for Pain
Jones, WOMAC
Fitzgerald, SF-36
Brander, KSS
1.78 (1.58, 1.97)
1.33 (1.06, 1.60)
1.58 (1.28, 1.88)
0
1
2
3
4
5
0.8

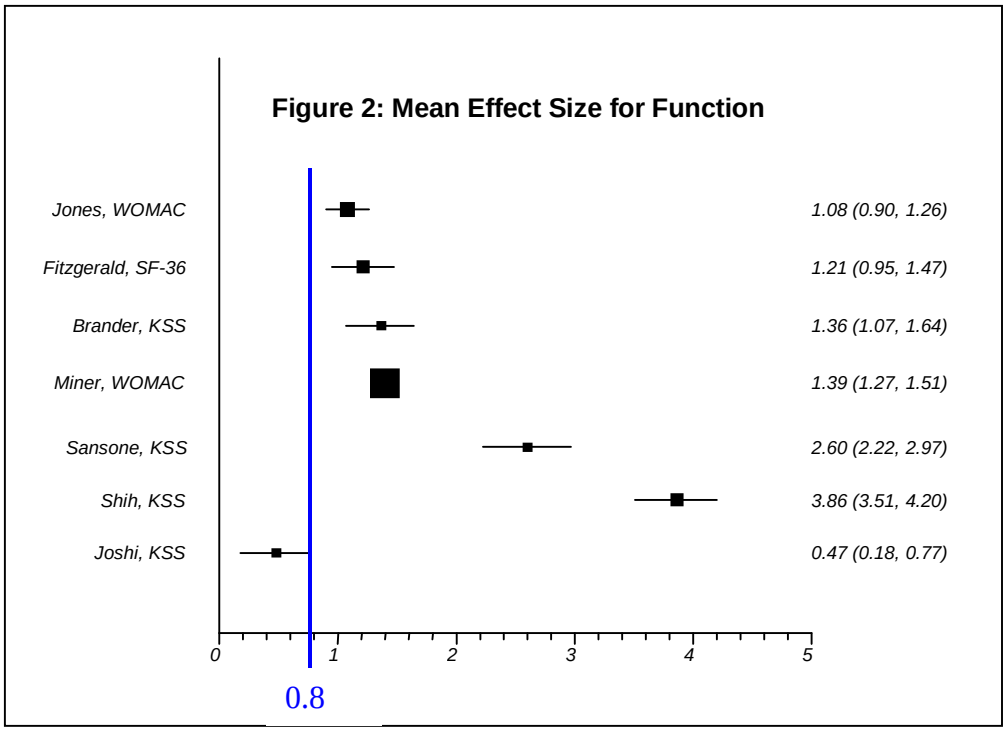


Figure 2: Mean Effect Size for Function
Jones, WOMAC
Fitzgerald, SF-36
Brander, KSS
Miner, WOMAC
Sansone, KSS
Shih, KSS
Joshi, KSS
1.08 (0.90, 1.26)
1.21 (0.95, 1.47)
1.36 (1.07, 1.64)
1.39 (1.27, 1.51)
2.60 (2.22, 2.97)
3.86 (3.51, 4.20)
0.47 (0.18, 0.77)
0
1
2
3
4
5
0.8

Figure 3: Mean Effect Size Overall

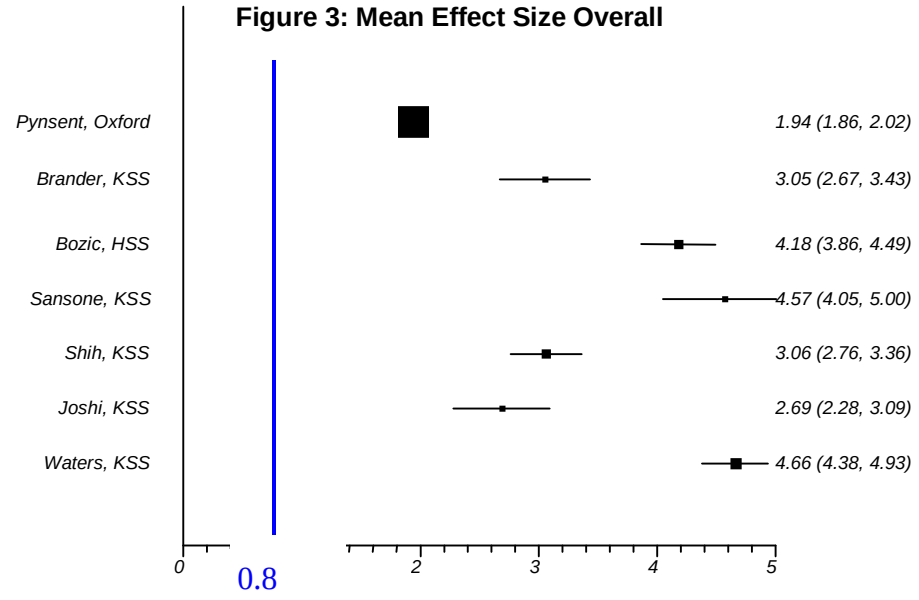


Table 5: Mean Effect Sizes for Preoperative and Postoperative Standardized Scores

Study	N/No. Knees*	Outcome Measure†	Function			Pain			Overall/Clinical‡		
			Preop Mean (SD or Range)	Postop Mean (SD or Range)	Effect Size	Preop Mean (SD or Range)	Postop Mean (SD or Range)	Effect Size	Preop Mean (SD or Range)	Postop Mean (SD or Range)	Effect Size
Less than 1 year follow-up											
Jones, 2003 (27)	276/ 276	WOMAC	42.8 (17.4)	70.5 (18.2)	1.56 (1.36–1.74)	43.4 (17.6)	76.0 (19.1)	1.78 (1.68–1.88)	—	—	—
1 year follow-up											
Pynsent, 2005 (34)	1739/ 1739	Oxford	—	—	—	—	—	—	68.8 (56.2–79.2)	29.2 (14.6–45.8)	-1.94 (1.86–2.02)
Fitzgerald, 2004 (24)	131/254	SF-36	35.9 (23.1)	67.0 (28.0)	1.21 (1.01–1.41)	36.0 (18.3)	66.1 (26.2)	1.33 (1.06–1.60)	—	—	—
March, 2004 (30)	153/209	WOMAC	37	23	N/A	10.5	5.5	N/A	—	—	—
Pagnano, 2004 (33)	240/240	KSCRS	51 (0–90)	89 (60–100)	N/A	36 (12–60)	92 (70–100)	N/A	—	—	—
Sorrells, 2004 (38)	282/ 371	NJOH	10	24	N/A	12	25	N/A	—	—	—
Brander, 2003 (22)	116/149	KSCRS	46.1 (0–90)	75 (5–100)	1.44 (1.15–1.72)	52.6 (24.4)	16.6 (21.0)	1.58 (1.43–1.73)	45.4 (16.3)	89.7 (12.5)	3.05 (2.66–3.42)
Hassaballa, 2003 (26)	106/113	Oxford	—	—	—	6.76	14.58	N/A	—	—	—
Miner, 2003 (32)	684/684	WOMAC	46.4 (18.4)	73.5 (20.6)	1.39 (1.27–1.50)	—	—	—	—	—	—
2 to 5 years follow-up											
Hassaballa, 2003 (26)	106/113	Oxford	—	—	—	6.76	15.45	N/A	—	—	—
Meding, 2003 (31)	291/329	KSCRS diabetics	41	76	—	10	46	N/A	47	88	N/A
	3228/ 4891	KSCRS non-diabetics	49	89	—	9	41	N/A	39	79	N/A
Ritter, 2003 (35)	3998/ 6200	KSCRS	—	—	—	—	—	—	50.0	89.2	N/A
5 or more years follow-up											
Bozic, 2005 (23)	248/287	HSSK	—	—	—	—	—	—	46.7 (11.3)	91.3 (10.0)	4.18 (3.86–4.49)
Goldberg, 2004 (25)	99/124	KSCRS	28 (10–45)	85 (50–100)	N/A	—	—	—	31 (0–47)	91 (72–100)	N/A
Kim, 2004 (29)	190/380	KSCRS	—	—	—	—	—	—	26.9 (3–63)	89.7 (45–100)	—
Sansone, 2004 (36)	102/110	KSCRS	45 (12.6)	74 (9.5)	2.60 (2.22–2.96)	—	—	—	33 (12.8)	82 (8.1)	4.57 (4.04–5.08)
Shih, 2004 (37)	187/235	KSCRS	58 (7)	87 (8)	3.86 (3.51–4.19)	—	—	—	67 (7)	90 (8)	3.06 (2.76–3.35)
Bankes, 2003 (21)	194/198	KSCRS	31.3 (10–60)	75.2 (40–100)	—	—	—	—	28.5 (10–60)	76.4 (52–97)	—
Joshi, 2003 (28)	90/110	KSCRS	39 (19.9)	51 (29.8)	0.47 (0.18–0.77)	—	—	—	40 (12)	86 (21)	2.69 (2.27–3.08)
Ritter, 2003 (35)	3998/ 6200	KSCRS	—	—	—	—	—	—	50.0	80.6–90.6	N/A
Waters, 2003 (39)	390/474	KSCRS	—	—	—	—	—	—	44.1 (13.1)	91.4 (5.9)	4.66 (4.39–4.92)

*N/No. Knees: This column reports the total number of participants in a study (N), then the number of knees that were included in the study (in some studies patients with bilateral TKR were included).
†HSSK indicates Hospital for Special Surgery knee scale; KSCRS, Knee Society Clinical Rating Scale; NJOH, New Jersey Orthopaedic Hospital score; Oxford, Oxford Knee Rating Scale; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index
‡KSCRS reports a 'clinical score' which combines measures of pain, stability, range of motion; the KSCRS 'function score' is based on the how the patients perceives that the knee functions during specific activities.

Percent Change

As discussed, a 20% change between preoperative and postoperative measurement scores is considered a minimally clinically important difference. Based on the studies in this review that reported preoperative and postoperative measurement scores, TKR improves overall outcome and function scores (Table 6 on the next page). The range of percent change for overall outcome scores was 34% to 233%; for function, the range was 31% to 204%. The study by Joshi et al. (28) reported the lowest percent change in function score; however, this study included patients aged 80 years and older. Nonetheless, a 31% improvement in function after TKR is a clinically important difference. The percent change is reported in Table 6 for the studies that reported preoperative and postoperative outcome scores.

For pain, the Medical Advisory Secretariat defined a meaningful decrease as at least 33%. Eight studies reported preoperative and postoperative pain scores. The range in pain reduction was 75% to 360%. Thus, all studies found a meaningful decrease in pain after TKR.

As mentioned previously, it is important to interpret these findings cautiously, because none of these studies were designed to measure the effectiveness of TKR even though all reported preoperative and postoperative scores. In addition, the percent change outcome does not take into account the sample size or the standard deviation.

Table 6: Percent Change Between Preoperative and Postoperative Standardized Scores

Study	N/No. Knees*	Outcome Measure†	Function			Pain			Overall		
			Preop, Mean (SD or Range)	Postop, Mean (SD or Range)	% Change	Preop, Mean (SD or Range)	Postop, Mean (SD or Range)	% Change	Preop, Mean (SD or Range)	Postop, Mean (SD or Range)	% Change
Less than 1 year follow-up											
Jones, 2003 (27)	276/276	WOMAC	42.8 (17.4)	70.5 (18.2)	65.0	43.4 (17.6)	76.0 (19.1)	75.0	—	—	—
1 year follow-up											
Pynsent, 2005 (34)	1739/ 1739	Oxford	—	—	—	—	—	—	68.8 (56.2–79.2)	29.2 (14.6–45.8)	136
Fitzgerald, 2004 (24)	131/254	SF-36	35.9 (23.1)	67 (28)	87	36.0 (18.3)	66.1 (26.2)	84	—	—	—
March, 2004 (30)	153/209	WOMAC	37.0	23.0	38.0	10.5	5.5	91.0	—	—	—
Pagnano, 2004 (33)	240/240	KSCRS	51 (0–90)	89 (60–100)	75	36 (12–60)	92 (70–100)	156	—	—	—
Sorrells, 2004 (38)	282/371	NJOH	10	24	140	12	25	108	—	—	—
Brander, 2003 (22)	116/149	KSCRS	46.1 (0–90)	75 (5–100)	63	52.6 (24.4)	16.6 (21.0)	217	45.4 (16.3)	89.7 (12.5)	98
Hassaballa, 2003 (26)	106/113	Oxford	—	—	—	6.76	14.58	116	—	—	—
Miner, 2003 (32)	684/684	WOMAC	46.4 (18.4)	73.5 (20.6)	58	—	—	—	—	—	—
2 to 5 years follow-up											
Hassaballa, 2003 (26)	106/113	Oxford	—	—-	—	6.76	15.45	129	—	—	—
Meding, 2003 (31)	291/329	KSCRS (diabetics)	41	76	85	10	46	360	47	88	87
	3228/ 4891	KSCRS (non-diabetics)	49	89	76	9	41	355	39	79	102
Ritter, 2003 (35)	3998/ 6200	KSCRS	—	—	—	—	—	—	50.0	89.2	78
5 or more years follow-up											
Bozic, 2005 (23)	248/287	HSSK	—	—	—	—	—	—	46.7 (11.3)	91.3 (10.0)	96
Goldberg, 2004 (25)	99/124	KSCRS	28 (10–45)	85 (50–100)	204	—	—	—	31 (0–47)	91 (72–100)	194
Kim, 2004 (29)	190/380	KSCRS	—	—	—	—	—	—	26.9 (3–63)	89.7 (45–100)	233
Sansone, 2004 (36)	102/110	KSCRS	45 (12.6)	74 (9.5)	64	—	—	—	33 (12.8)	82 (8.1)	149
Shih, 2004 (37)	187/235	KSCRS	58 (7)	87 (8)	50	—	—	—	67 (7)	90 (8)	34
Bankes, 2003 (21)	194/198	KSCRS	31.3 (10–60)	75.2 (40–100)	140	—	—	—	28.5 (10–60)	76.4 (52–97)	168
Joshi, 2003 (28)	90/110	KSCRS	39 (19.9)	51 (29.8)	31	—	—	—	40 (12	86 (21)	115
Ritter, 2003 (35)	3998/ 6200	KSCRS	—	—	—	—	—	—	50.0	80.6–90.6	61
Waters, 2003 (39)	390/474	KSCRS	—	—	—	—	—	—	44.1 (13.1)	91.4 (5.9)	107

*N/No. Knees: This column reports the number of participants in a study (N), then the number of knees that were included in the study (in some studies patients with bilateral TKR were included).
†HSSK indicates Hospital for Special Surgery knee scale; KSCRS, Knee Society Clinical Rating Scale; NJOH, New Jersey Orthopaedic Hospital score; Oxford, Oxford Knee Rating Scale; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Revision Rates and Failure of Prosthesis

Nine of the 19 studies that reported preoperative and postoperative outcome scores also reported revision rates. Table 7 outlines the details of those revisions. The rates of revision ranged between 0% and 13% in studies that reported more than 5 years of follow-up data. The data shown in Table 7 are for revisions only. Patients may experience complications related to their knee replacement, but not undergo revision surgery to alleviate the complication.

The OJRR has only recently started collecting data (since 2001); therefore, it does not have long-term

data to assess the revision rates or the duration of effect of the prostheses. The Swedish Knee Arthroplasty Register is the most established knee replacement registry worldwide. It has been collecting data on knee replacements since the mid 1970s (http://www.ort.lu.se/knee/indexeng.html). They report that there has been an improvement in the rates of revisions over time, because the TKR surgeries that were done between 1978 and 1983 were associated with the highest rates of revision, regardless of time since surgery. That is, even at 4 years after surgery, the Swedish Registry reported that the rates of revision were higher for the TKR procedures between 1978 and 1983 than for any other period. (40)

Table 7: Rates of Revisions in the Studies That Reported Preoperative and Postoperative Outcome Scores

Study	N/No. Knees	No. Revisions	Revision Rate, %	Time of Revision	Reason for Revision (No. Patients)
Less than 1 year follow-up					
Jones, 2003 (27)	276/276	NR†			
1 year follow-up					
Pynsent, 2005 (34)	1739/1739	NR			
Fitzgerald, 2004 (24)	131/254	NR			
March,2004 (30)	153/209	NR			
Pagnano, 2004 (33)	240/240	NR			
Sorrells, 2004 (38)	282/371	29	5.5	< 5 years (19 pts)† 5–12 years (10 pts)	• Component malposition (8) • Tibial component subsidence (4) • Deep infection (3) • Bearing malrotation (2) • Ligament laxity (2) • Cosmetic deformity (1) • Patellar component baja (1) • Component wear (5) • Adhesions (1) • Aseptic tibial loosening (1) • Osteolysis (1)
Brander, 2003 (22)	116/149	1	0.8	6 months	• Acute patella fracture
Hassaballa, 2003 (26)	106/113	NR			
Miner, 2003 (32)	684/684	NR			
2-5 years follow-up					
Hassaballa, 2003 (26)	106/113	NR			
Meding, 2003 (31)	291/329	12	3.6	NR	• Aseptic loosening (all)
	3228/ 4891	20	0.4		
Ritter, 2003 (35)	3998/ 6200	NR			
5 or more years follow-up					
Bozic, 2005 (23)	248/287	9	3.1	2 weeks to 65 months	• Hematoma (3) • Heterotopic ossification (1) • Complex pain syndrome (1) • Periprosthetic fracture (1) • Infection (1) • Midflexion instability (1) • Aseptic loosening (1)
Goldberg, 2004 (25)	99/124	15	13.0	Mean, 5.4 years	• Component wear (NR) • Polyethylene delamination (NR) • Peg failure (NR) • Tibial loosening (1) • Deep infection (1)
Kim, 2004 (29)	190/380	0	0	—	—
Sansone, 2004 (36)	102/110	7	6.9	Within first 3 years	• Instability (2) • Aseptic loosening (1) • Traumatic dislocation (1) • Intractable patellar pain (2) • Periprosthetic ossification (1)
Shih, 2004 (37)	187/235	NR			
Bankes, 2003 (21)	194/198	2	1.0	4 and 6 years	• Deep infection (2)
Joshi, 2003 (28)	90/110	0	0	—	—
Ritter, 2003 (35)	3998/6200	NR			
Waters, 2003 (39)	390/474	NR			

*N/No. Knees: This column reports the total number of participants in a study (N), then the number of knees that were included in the study (in some studies patients with bilateral TKR were included).
†NR indicates not reported; pts, patients.

Factors Related to Outcomes for Total Knee Replacement

Six studies (27;41-45) were identified that investigated factors related to outcomes for TKR using regression analyses. There was variation in the variables included in the analyses. The generally accepted rule regarding the sample size for a regression analysis is 10 subjects per variable. For instance, a regression analysis incorporating 10 variables should have a minimum sample size of 100. Two studies (43;44) did not meet this requirement.

Table 8 on the next page shows the features of the analyses. The proportion of variance explained by the models was low. Parent et al. (43) reported that they were able to explain 66% of the variance; however, they had 18 variables in their model and only 65 patients. The other models were able to predict between 12% and 28% of the variance with their models, which is very low. All of the regression analyses investigated factors that predicted function, and 2 also investigated factors that predicted pain. Both of these studies used the WOMAC pain score as their independent variable. Three of the analyses used the WOMAC function score to predict function, 1 used extension and flexion, and another used locomotor ability.

Table 8: Multivariate Analyses of Factors To Predict Pain and Function in Patients Undergoing Total Knee Replacement

Study	N	Predictor Outcome of Interest	Time of Modeling	No. Variables in Analyses	Variance Explained by Model, %	Adequate Sample Size for the No. Variables in Model?
Collier, 2004 (41)	147	Extension and flexion	NR	11	12	Yes
Lingard, 2004 (42)	860	WOMAC pain and function	24 months postop	10	Pain: 12 Function: 25	Yes
Jones, 2003 (27)	276	WOMAC function	6 months postop	16	27	Yes
Parent, 2003 (43)	65	Locomotor ability	2 months postop	18	66	No
Jones, 2001 (45)	257	WOMAC pain and function	6 months postop	Pain: 7 Function: 10	Pain: 18 Function: 28	Yes
Sharma, 1996 (44)	47	SF-36 physical functioning	3 months postop	12	27	No

The variables that were included in the studies are listed in Table 9. The grey boxes indicate that the variable was not analyzed in the study, the boxes with Xs indicate that the variable was included in the study but was not a predictor of the outcome, and the boxes with checkmarks indicate that the variable was included in the study and was a significant predictor of outcome (and thus included in the final model). The 2 studies (43;44) that did not include a sufficiently large sample size in their regression analyses were excluded from the table.

Table 9: Multivariate Analyses Identifying Predictors of Function and Pain After Total Knee Replacement

Variable*	Lingard, 2004 (N = 860)	Jones, 2001 (N = 257)	Collier, 2003 (N = 238)	Jones, 2001 (N = 257)	Jones, 2003 (N = 276)	Lingard, 2004 (N = 860)
Predictor of:	WOMAC pain	WOMAC pain	Flexion/ extension	WOMAC function	WOMAC function	WOMAC function
% of variance explained	12	18	12	28	27	25
Age	×	×	✓	×	×	×
Gender	✓	×	✓	×	✓	×
Body mass index	×		×	×	×	×
Activity level			✓			
Lives alone				×	×	
Education	×					×
Income	×					×
Unemployed	×					×
Comorbidities	✓	×		×	✓	✓
Diagnosis					×	
Waiting time		×		×	×	
Length of hospital stay		✓		✓	×	
Prior surgery (non-TKR)			×		×	
Walking distance					×	
Walks with device					✓	
Unilateral vs. bilateral				×		
Range of motion			✓		×	
Osteoarthritis severity			×			
Instability			×			
Cemented device		✓			×	
Preop function: KSCRS			×			
Preop function: SF-36					×	
Preop pain: WOMAC	✓			✓	×	✓
Preop pain: SF-36		✓		×		

* TKR indicates total knee replacement; KSCRS, Knee Society Clinical Rating Scale; SF-36 Short-form 36; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Overall, the regression analyses accounted for less than one-third of the variance. This suggests that there are variables that predict pain and function outcomes after TKR that the analyses missed.

Obesity as a Predictor of Outcome After Total Knee Replacement

Five studies (46-50) were identified that investigated obesity as a predictor of adverse outcomes after

TKR. Table 10 outlines the features of these studies. BMI was used in the studies to define obesity.

Table 10: Characteristics of Studies Investigating Obesity as a Predictor of Adverse Outcomes After Total Knee Replacement

Study		N/No. Knees	Age, Mean (SD or Range)	Female, %	OA, %	Definition of Obese	BMI,* Mean (SD; Range)	Type of device	Follow-up, Mean Years (Range)
Foran, 2004 (47)	Case	68/78	66 (8.6)	79	NR*	BMI ≥ 30	35.3 (4.2; 30.0–47.0)	36 knees cemented 42 knees hybrid	6.7 (5.0–10.3)
	Control	68/78	70 (7.9)	64			26.2 (2.5; 17.6-29.8)	40 knees cemented 38 knees hybrid	6.9 (5.0–10.3)
Foran, 2004 (46)	Case	27/30	59 (36–71)	37	97	BMI ≥ 30	34 (30–45)	Porous-coated anatomic prosthesis (cementless)	14.5 (7.7–8.3)
	Control	27/30	62 (36–78)	37	97		27 (21–29)		15.4 (8.3–18.4)
Deshmukh, 2002 (48)		180/180	69 (40–89)	53	100	< 25 healthy 25–29.9 overweight 30–39.9 obese > 40 morbidly obese	28 (18.5–44.5)	Cemented Kinemax prosthesis	> 1
Spicer, 2001 (49)	Case	285/326	64.6 (35–83)	62	NR	BMI ≥ 30	NR	PFC, posterior cruciate retaining TKR with patellofemoral resurfacing	6.3 (4–12)
	Control	371/425	69.7 (35–83)	59					6.1 (4–12)
Stickles, 2001 (50)		1011/NR	69.9 (18–95)	NR	100	<25 healthy 25–29.9 overweight 30–34.9 obese I 35–39.9 obese II >40 obese III	31.2 (6.8–59.9)	NR	> 1

*BMI indicates body mass index; NR, not reported.

Stickles et al. (50) compared outcomes of patients undergoing TKR according to their BMI, which was divided into 5 categories: less than 25, 25 to 30, 30 to 35, 35 to 40, and more than 40. The study did not report any significant differences in outcomes according to BMI.

The case-control study by Spicer et al. (49) compared patients undergoing TKR who had BMIs over 30 to a control group of patients undergoing TKR who had BMIs less than or equal to 30. After a mean follow-up of 75.9 months (range, 48–144 months), the differences between the groups on changes in KSCRS scores were not statistically significant. The patients with a BMI over 30 had a revision rate of 4.9% compared to 3.1% in the patients with a BMI less than or equal to 30 (P = .25). Spicer et al. also found that the 10-year survival rate was not statistically significantly different between the groups.

Similar to the studies by Spicer et al. (49) and Stickles et al., (50) the study by Deshmukh et al. (48) found that body weight did not adversely affect the outcome of TKR. They conducted a regression analysis to model BMI using the following variables: age, sex, extent of arthritis, comorbidities, and severity of disease based on baseline KSCRS and Nottingham Health Profile scores. They found that none of the

variables dominated the model to explain the variance.

Two separate studies by Foran et al. (46;47) reported that obesity did adversely affect the outcome of TKR. Both were case-control studies, comparing the outcomes of obese patients (BMI $\geq$ 30) to outcomes of not obese patients (BMI < 30) undergoing TKR. Table 11 compares the characteristics of these 2 studies. Unfortunately, Foran et al. did not report power calculations in either study. In the Foran et al. (47) study with 68 patients in each group, the mean postoperative KSCRS score in the obese group was 90 compared to 94 in the non-obese group. Foran et al. indicated that there was a significant difference between these scores (P = .04); however, this difference was not clinically significant, because a KSCRS score of more than 85 is considered excellent.

The other study by Foran et al. (46) had only 27 patients in each group and reported inconsistencies in the number of failures in each group. They reported 3 failures in the non-obese group and 10 failures in the obese group; however, they reported more revisions in the non-obese group (18 revisions) than in the obese group (10 revisions). The data used for this study were from 1982 to 1986. There have been substantial improvements in knee replacement technologies and procedures in the past 20 years, which makes the results of this study less relevant.

Table 11: Comparison of Foran et al.'s Studies Measuring Obesity as a Predictor of Adverse Outcomes After Total Knee Replacement

Study	**Foran et al., 2004 (46)**		**Foran et al., 2004 (47)**	
Type of study	Case-control		Case-control	
Recruitment years	1982–1986		1991–1996	
Definition of obese	BMI* $\geq$ 30		BMI $\geq$ 30	
	Obese	Non-obese	Obese	Non-obese
N (no. knees)	27/30	27/30	68/78	68/78
Age, mean years (range)	62 (36–78)	59 (36–71)	66 (32–84)	70 (42–84)
Female, %	41	41	79	64
BMI, mean (range or SD)	34 (30–45)	25 (21–29)	35.3 (4.2)	26.2 (2.5)
Follow-up, mean years (range)	14.5 (7.7–18.3)	15.4 (8.3–18.4)	6.7 (5.0–10.3)	6.9 (5.0–10.3)
Preoperative KSCRS,* mean (range)	38 (10–65)	42 (17–62)	59 (31–80)	57 (30–82)
	P = .23		P = .14	
Postoperative KSCRS, mean (range)	81 (30–98)	89 (30–98)	90 (40–100)	94 (62–100)
	P = .02		P = .04	
Mean change in KSCRS (range)	43	47	31 (-33 to +65)	37 (+6 to +70)
	P = NR*		P = .01	

*BMI indicates body mass index; KSCRS, Knee Society Clinical Rating Scale; NR, not reported.

Thus, 5 studies were identified that specifically examined the effect of weight on the outcome of TKR, 3 studies, each with well over 100 patients and follow-up periods greater than 1 year, reported that weight did not affect the outcome of TKR. Two studies, by the same group of authors, found that weight was a significant predictor of TKR outcomes; however, both studies had several limitations.

Timing of Total Knee Replacement Surgery and Outcomes

Three studies (51-53) (2 non-RCTs with contemporaneous controls and 1 retrospective review) were identified that investigated the role of degree of severity on the outcomes of TKR. The original comparative study was published in 1999, (52) and an update of the study was published in 2002. (54)

Firstly, it is important to recognize that all 3 studies defined severity of osteoarthritis differently. The study by Gidwani et al. (51) defined severity according to Ahlback's grading scale for osteoarthritis. The review by Meding et al. (53) used radiological images. The study by Fortin et al. (52) used the WOMAC function score to separate patients into high and low functioning groups (divided at the median score). Thus, it is difficult to compare the outcomes of the 3 studies because they used different criteria to assess severity.

Gidwani et al. (51) tested the hypothesis that TKR in "patients with relatively early stages of osteoarthritis will lead to a poor outcome." This prospective case series included 130 patients with osteoarthritis undergoing TKR. X-rays were used to determine the severity of osteoarthritis before surgery using the Ahlback Radiologic Classification of Osteoarthritis of the Knee scale. The scale ranges from 0 to 5, where 0 is a healthy knee, and 5 indicates "gross bone loss and subluxation." Most knees were rated 2 or 3 (80% of patients). The knees were divided into 2 categories based on severity. All knees with scores of 0 to 2 were placed in group A, and the knees that scored 3 to 5 were placed in group B.

Oxford Knee Scores were taken preoperatively and postoperatively in all patients. It is important to note that the median preoperative scores were similar for patients with "severe" disease and those with "less severe" disease. The median preoperative Oxford score for group A was 38; for group B, it was 33. At 1 year the median postoperative Oxford score for group A was 74; for group B, it was 75.

Gidwani et al. also reported the mean change in Oxford scores in 1-year postoperative scores compared with preoperative scores for knees based on Ahlback grades. Knees categorized as grade 1 improved 40%; grade 2, 34%; grade 3, 38%; and grade 4, 32%. It is important to recall that most of the knees were categorized as grade 2 or 3, and only 6 knees were included in the grade 1 subgroup. Nonetheless, patients improved substantially regardless of their initial severity grade. Gidwani et al. proposed that the results of their study supported the conclusion that TKR could be effectively performed earlier in patients with osteoarthritis, thereby preventing some of the pain and discomfort associated with more severe grades of osteoarthritis.

Meding et al.'s retrospective study (53) of 1888 patients comprising 2759 consecutive TKR surgeries reported similar findings to the study by Gidwani and colleagues. As mentioned previously, Meding et al. determined severity based on radiological images. If there was evidence of bone touching bone in 1 or more compartments of the knee, then the patients was categorized as "severe;" otherwise, the patient was categorized as mild. Meding et al. reported that there were no significant correlations between the severity of osteoarthritis (mild versus severe) and Knee Society overall knee scores, function scores, or pain scores at 1 year, 3 years, 5 years, or 7 years postoperatively.

Fortin et al.'s study (52) included 222 patients undergoing total joint replacement (n = 106 knee replacement patients). Fortin et al included patients with earlier intervention in Boston to later intervention in Montreal. Patients were divided into high or low function groups based on their WOMAC

function scores (Table 12). There were more knees in the high function group, and there were more male patients in this group. Fortin et al. reported 2 measures for comorbid conditions. Both indicated that the groups were evenly matched for comorbid conditions. The Comorbidity Illness Rating Scale is more sensitive to disabling conditions than the Charlson Index, and the Charlson Index is more sensitive to life-threatening conditions. Patients were recruited from a hospital in Montreal and a hospital in Boston. Canadians had poorer functioning than did American.

Table 12: Comparing High and Low Function Groups in Fortin et al. (52)

Variable	High Function	Low Function
Number of knees	59	47
Age, mean years (SD)	67.9 (9.7)	66.0 (8.2)
Male, %	54	32
Mean years of education (SD)	14.1 (3.2)	12.5 (4.0)
Comorbidity Illness Rating Scale	3.0	3.0
Charlson Index of Comorbidities	0.0	0.0

Fortin et al. found that patients who had low functioning before surgery had bigger differences between their preoperative and postoperative function scores compared with those who had higher functioning preoperatively. Nonetheless, the patients with low functioning preoperatively did not improve as much as did patients with high functioning. The mean preoperative WOMAC function score was 44.2, and the mean postoperative WOMAC function score at 6 months was 23.0 for the low functioning group (in this study higher WOMAC scores mean poorer functioning), a difference of 21.2. For the high function group, the preoperative WOMAC function score was 24.3, and the mean postoperative score at 6 months was 9.5, a difference of 14.8. A similar trend was observed on the WOMAC pain scores as well, where the difference in pain was greater in the low functioning group; however, they did not have a large enough reduction in pain to "catch up" with the high functioning group. Fortin et al. only reported results up until 6 months postoperatively.

Subsequently, Fortin et al. (54) reported results for the aforementioned study with 2 years of follow-up data. There were 165 (74%) patients who had had total hip or knee replacement surgery still in the study 2 years later. Of these, 81 (76%) patients remained who had had TKR. Fortin et al. reported that the 57 total hip and knee replacement patients that were missing had similar baseline characteristics as the remaining patients for age, sex, education, comorbid conditions, baseline function and pain scores, type of joint replacement, and centre where the surgery took place.

Figures 4 and 5 chart the change in WOMAC scores for function and pain, respectively, from baseline to 6 months to 24 months postoperatively. Fortin et al. did not report any results of statistical comparisons between the low and high function groups. When the Medical Advisory Secretariat calculated the mean difference in the scores (t-tests), they found a significant difference between the scores at all time periods (baseline, 6 months, and 24 months) for pain and function ($P < .001$).

This study indicates that the high functioning patients did better overall than did the low functioning patients in terms of pain relief and improved functioning. Patients allowed to deteriorate by waiting too long for their surgery improve after total hip or knee joint replacement surgery, but at two years post-

operatively have significantly poorer pain relief and functional improvement than patients who receive surgery in a more timely manner.

Figure 4: Change in WOMAC Function Score in Low and High Function Groups in Fortin et al. (52;54)

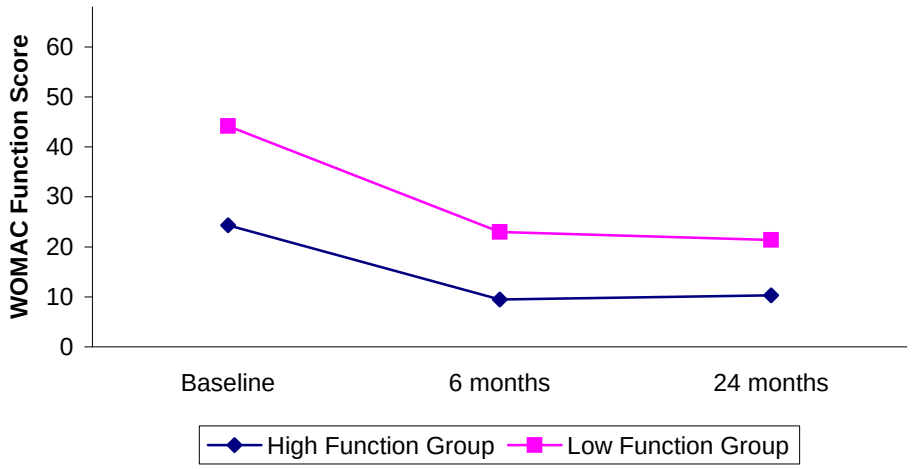
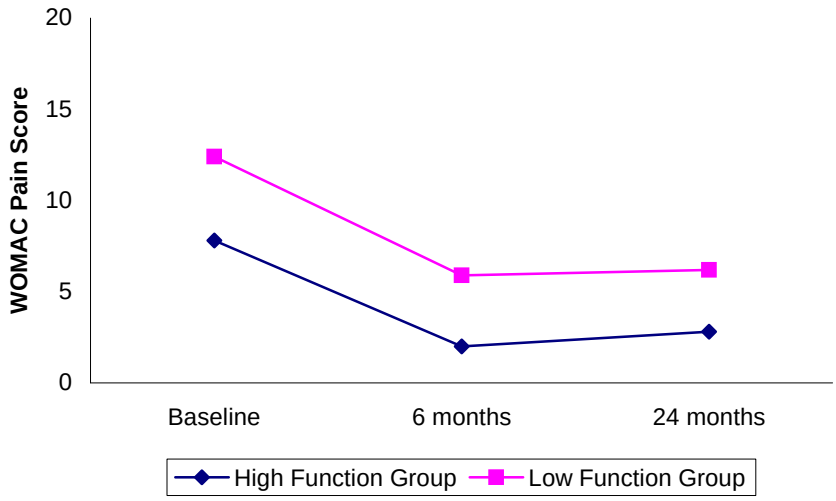


Figure 5: Change in WOMAC Pain Score in Low and High Function Groups in Fortin et al. (52;54)



Unicompartmental Knee Replacement

UKR is considered for patients who have isolated medial compartment arthritis and at least 120 degrees of knee flexion. It is usually reserved for patients aged over 60 years (Personal communication, April 25, 2005).

The Medical Advisory Secretariat reviewed the literature with the aim of investigating if UKR is safe and effective compared with TKR. In particular, rates of revisions and complications were scrutinized. Four studies (26;55-57)
(1 RCT, 2 prospective matched case series, 1 retrospective review) were identified that compared unicompartmental knee replacement to TKR.

Newman et al. randomized 94 patients (comprising 102 knees) who met the indications for UKR to receive either UKR or TKR. The groups were evenly matched on age, sex, preoperative range of motion, and preoperative Bristol Knee Score. Eleven patients (52 knees) in the TKR group had hospital stays longer than 20 days, compared with 3 patients (50 knees) in the UKR group.

Patients were followed-up at 8 months, 2 years, and 5 years. At 8 months, 5 patients in the TKR group had deep venous thrombosis. Only 1 patient in the UKR group had this condition. At 5 years, the mean change (improvement) in the Bristol Knee Score was 67% for patients in the UKR group and 52% for patients in the TKR group. Regarding pain, 89% of the patients in the UKR group reported that pain relief was "excellent" compared with 83% of patients in the TKR group. Three revisions were reported: 2 in the UKR group (at 20 months and 57 months) and 1 in the TKR group (at 60 months). There were no data on the statistical significance, if any, between the 2 treatment arms. The authors did, however, conclude that UKR was superior in a specified population. They did not report any power calculations, so it is not possible to determine if the study was powered sufficiently to detect a difference between the groups.

The retrospective study by Weale et al. (55) compared the patient records of patients who had had TKR (n = 104) with those who had had UKR (n = 28). The patients who had had UKR (mean, 62.4 years) were younger than those who had undergone TKR (mean, 71.3 years). The indications for UKR were as follows:

- Stage I–III arthritis on the Ahlback radiologic classification
- The varus deformity had to be correctable passively to neutral
- Anterior cruciate ligament was intact intraoperatively
- Cartilage of the lateral compartment was normal

The patients that did not meet the criteria for UKR received TKR. Thus, comparing UKR to TKR in this study was not appropriate, because the groups were not comparable. Nonetheless, Weale et al. made comparisons based on pain and functional outcomes. The mean follow-up was 2.3 years (SD, 1 year). There were no significant differences in mean follow-up scores on the Oxford Knee Scale. Patients who had had UKR spent significantly fewer days in hospital than those who had had TKR (10.6 days versus 14.4 days, $P < .001$).

Hassaballa et al. (26) did a prospective study and measured the preoperative kneeling ability of the patients who were to receive wither UKR or TKR. About 87% of the patients undergoing TKR and 83% of patients undergoing UKR reported preoperatively that they could not kneel or that it was extremely difficult to kneel. One year postoperatively, 41% of the patients in the TKR group and 53% of the patients in the UKR group reported better kneeling ability. Hassaballa et al. did not report the specific Oxford Knee Score pain scores, but they did state that there was no difference at 1 year postoperatively in pain between patients who had had UKR those who had had TKR ($P = .51$). The one area where there was a

significant difference between patients in the UKR and TKR groups was the ability to climb stairs. Significantly more patients in the UKR group were able to climb stairs 1 year postoperatively ($P = .02$). However, at 2 years postoperatively, there was no difference between the groups in the ability to climb stairs ($P = .12$).

The prospective matched-pair comparison study by Yang et al. (56) compared 50 consecutive patients undergoing UKR to 50 patients undergoing TKR. All patients had to be older than 50 years old, have "active community ambulation," radiological evidence of medial compartmental osteoarthritis only, absence of patella-femoral symptoms, competence of both cruciate ligaments, less than 15 degrees varus, and absence of fixed flexion deformity. Patients were matched according to age, preoperative range of motion, and radiological grade of knee arthrosis. At 6 months, patients who underwent UKR had significantly better recovery outcomes compared to those who underwent TKR in terms of faster rehabilitation, earlier ambulation, shorter length of hospital stay, and better postoperative range of motion ($P < .01$).

Summary of Findings of Literature Review

As mentioned earlier in the review, an *a priori* decision was made not to look at the types of devices and compare the differences between the devices in terms of surgical technique, fixation technique, or in variation of the design of the prosthesis. The main aim of the review was to establish if knee replacement is effective at decreasing pain and improving function. However, if as the systematic review was being conducted, it became evident that the differences in surgical technique, fixation technique, or variation of the design of the prosthesis were substantially affecting the effectiveness of the knee replacement, then the differences would be investigated.

All of the studies that reported preoperative and postoperative measurement scores for patients undergoing TKR surgery found that most of the patients improved after TKR surgery. Thus, the differences in surgical technique, fixation technique, or variation of the design of the prosthesis were not investigated. This is not to say that differences affecting effectiveness did not exist among these variables, only that it seems pain and functioning got better for patients who had TKR surgery regardless.

Overall, the literature supports the conclusions that people who have TKR surgery for osteoarthritis see substantial improvements in pain and function. Comparing the mean effect score and the percent change in 21 studies that reported preoperative and postoperative outcome scores for patients undergoing TKR supported the effectiveness of TKR. The 21 studies included patients of various ages and used a variety of prostheses and techniques to implant the device, and TKR effective in all of the studies. The revision rates ranged from 0% to 13% in the studies reporting at least 5 years of follow-up.

As for the factors that predict TKR outcomes, a variety were evaluated, including obesity, age, gender, prosthesis design, and surgical technique; however, none of these were shown to predict outcomes (pain and/or function) consistently across studies. However, the regression analyses that were done were only able to account for 12% to 27% of the variance, indicating that over 70% of the variance in the pain and function outcomes for TKR is unexplained.

In terms of the timing of TKR, 2 studies found that the severity of osteoarthritis is not a predictor of outcome, but 1 study found that higher functioning patients had better functional outcomes up to 2 years after surgery compared to lower functioning patients. It is important to note that the patients in the low and high functioning groups were evenly matched in terms of comorbid conditions and age.

UKR surgery seems to be as effective as TKR surgery for people who meet the indications for it. This is a

subset of people who have osteoarthritis of the knee, because for UKR to be indicated, only 1 (usually the medial) compartment of the knee can be affected. Patients who undergo UKR surgery seem to have shorter hospital stays and faster recovery times than do patients who have TKR surgery.

Economic Analysis

Disclaimer: This economic analysis represents an estimate only, based on assumptions and costing methodologies that have been explicitly stated. These estimates will change if different assumptions and costing methodologies are applied for the purpose of developing implementation plans for the technology.

Literature Review on Economics

At the American College of Rheumatology Annual Scientific Meeting in 2004, Hawker et al. (58) presented an abstract on the cost-effectiveness of total joint replacement using Ontario data. They measured the osteoarthritis costs for patients 1 year before joint replacement (minus 6 weeks leading up to replacement) and then for 1 year starting 6 months after joint replacement. This was done to exclude the costs associated with the actual joint replacement procedure. Hawker et al. found that, overall, the total health care utilization costs were not significantly different (preoperative versus postoperative costs); however, among patients living in urban areas and/or those who had higher education, there was a significant decrease in total health care utilization costs ($P < .05$). The osteoarthritis-related costs were significantly lower after total joint replacement than before surgery (mean difference $400 (CDN); range -$4,150 to $22,000; $P < .0001$).

Ontario-Based Economic Analysis

Device Costs

There are 5-10 manufacturers of knee replacement prostheses licensed by Health Canada. The average cost of a primary TKR prosthesis is $2000 CDN. The unicompartmental prosthesis is slightly more expensive at $2500 to $3000 CDN. This is owing to the lower demand for the UKR prostheses. The design of the knee replacement prosthesis is evolving, and there are ongoing attempts to improve the quality, effectiveness, and survivorship of the prostheses. This means there will continue to be fluctuations in the cost of the prostheses over time.

Hospital Costs

The cost per TKR has been estimated at $10,375.26 CDN. (This is a weighted average of the costs at academic and community hospitals.) This includes professional fees (for surgeons, anesthesiologists, nurses, and hospital administration staff), the costs of the device, imaging costs, in-hospital medications, laboratory services, and in-hospital physiotherapy and occupational therapy. The hospitalization costs are based on the Joint Policy and Planning Committee and the Ministry of Health and Long-Term Care's approved case costing methodology. (Table 13)

Table 13. Costing for Total Knee Replacement, based on 2005/06 inflationary-adjusted rates

Weighted average (academic/community) all-inclusive hospitalization cost for total knee replacement, including the cost of the device	$8,767.18
Additional medication	$330.75
Follow-up consultation	$171.82
OHIP costs (95.5% of TKR procedures are billed FFS)	$1,105.51
Total estimated cost	$10,375.26

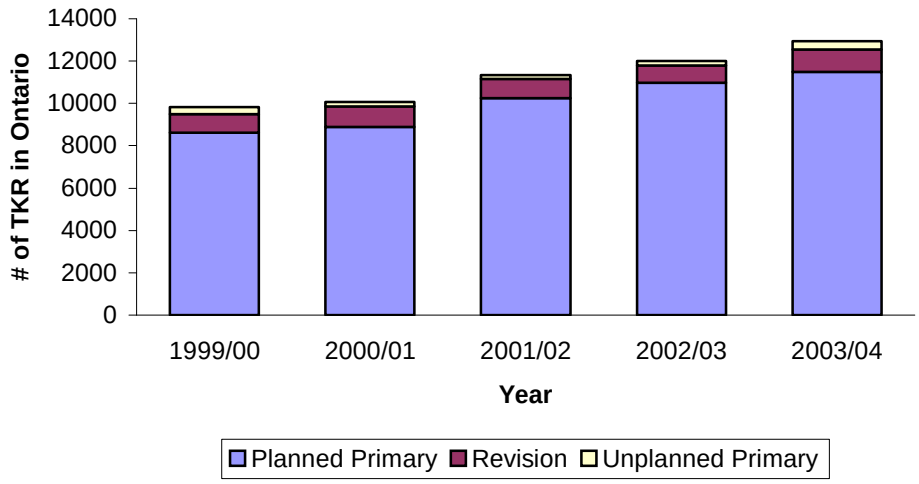
TKR is already well diffused as a procedure throughout Ontario. In 2003/2004 12,933 TKR surgeries were performed in Ontario. This figure includes revisions and unplanned primary TKR surgeries. Figure 6 shows the number of TKR surgeries in Ontario since 1999/2000. In 2005/2006, the estimated incremental volume of TKR procedures is 5,040; thus, the estimate for TKR surgeries in 2005/2006 is 17,973. (This includes planned primary knee replacement, unplanned primary knee replacement, and revisions.) Based on this figure, the total cost of TKR surgery in Ontario in 2005/2006 will be about $186 million (CDN). (Table 14)

Table 14. Estimated number of total knee replacements in Ontario in 2005/06

Estimated base number of TKR in 2003/04	12,933
Estimated incremental volumes of TKR (2004/05 & 2005/06)	5,040
Total	17,973
Estimated budget impact (2005) (cost per TKR * estimated number of TKR)	$186,474,525

The median waiting time for knee replacement in Ontario is 33 weeks. In 2003/2004 there were 5,824 people waiting for knee replacement surgery in Ontario.

Figure 6: Number of Total Knee Replacement Procedures Done in Ontario



Appraisal

Policy Considerations

Patient Outcomes – Medical, Clinical

TKR is an invasive procedure that requires a hospital stay of about 5 days. Nonetheless, the procedure is highly effective at reducing pain and improving function for people with severe osteoarthritis of the knee.

Ethics

Currently, the literature indicates that there is variation in when patients are referred for knee replacement. Without evidence-based indications for TKR, it is unclear when patients should be referred for knee replacement, thus causing great variation on when a patient receives knee replacement.

Demographics

Osteoarthritis affects more women than men: 61.3% of TKR surgeries in Ontario are for women according to the OJRR's 2004 annual report. (3) Osteoarthritis becomes more prevalent with age: 66% of the knee replacements are performed in patients between 65 and 84 years old. (3) In addition, osteoarthritis is more common in people who are overweight or obese. According to the OJRR's 2003 annual report, 84% of patients undergoing TKR were overweight or obese. (4)

Diffusion

TKR is already a well-diffused procedure. It is common practice throughout the province, Canada, and

the world. TKR surgery has been widely performed since the 1970s. The rate of TKR surgeries is increasing. Figure 7 indicates the increase in the demand for TKR over the past 5 years.

Cost

TKR surgery costs about $10, 375.26 CDN per patient. This covers all procedures associated with the 5-day hospital stay, including health professional costs, device costs, imaging costs, and the costs of laboratory services. The crude revision rate for Canada is about 8% (yearly number of revisions divided by the yearly number of revisions + primaries). (40)

Stakeholder Analysis

The median wait time for a TKR is 33 weeks in Ontario. The OJRR data suggests that people with more severe dysfunction receive their knee replacements sooner than do patients with less severe dysfunction. (3)

System Pressures

There are substantial system pressures related to knee replacement, including operating room time, availability of hospital beds, and the number of orthopedic surgeons in the province. There are also pressures associated with follow-up and aftercare of patients, including access to physiotherapists, rehabilitation hospitals, and the Community Care Access Centres.

Conclusions

There is substantial evidence to indicate that TKR effectively reduces pain and improves function.

An expert panel on osteoarthritis is meeting in the fall of 2005 to recommend strategies on the integration of the management of osteoarthritis. Some of the questions that the panel aims to answer include:

- Are there opportunities to reallocate funds from arthroscopic lavage and debridement or other procedures to TKR?
- What is the relationship between functional status prior to knee replacement and pain and function after surgery?
- What are the views of patients with respect to the risks and benefits of TKR?
- What are the complication rates from TKR and downstream costs associated with the complications?

Appendices

Appendix 1

Total Knee Replacement

Database: Ovid MEDLINE(R) <1966 to March Week 1 2005>
Search Strategy:
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1 exp Arthroplasty, Replacement, Knee/ (2849)
2 total knee replacement.mp. (625)
3 (total knee arthroscopy or tkr or tka).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (623)
4 or/1-3 (3062)
5 exp treatment outcome/ (142113)
6 exp "Recovery of Function"/ (5643)
7 exp "Outcome and Process Assessment (Health Care)"/ (158379)
8 exp Prosthesis Failure/ (3993)
9 exp Reoperation/ (12909)
10 exp Postoperative Complications/ (63239)
11 exp "Range of Motion, Articular"/ (6924)
12 exp follow-up studies/ (85953)
13 exp Survival Analysis/ (35989)
14 exp Risk Factors/ (117204)
15 Comparative Study/ (309843)
16 or/5-15 (629063)
17 4 and 16 (2192)
18 limit 17 to (humans and English language and yr=2002-2003) (742)
19 limit 18 to systematic reviews (23)
20 18 (742)
21 limit 20 to meta analysis (8)
22 20 (742)
23 limit 22 to (case reports or comment or editorial or letter or "review" or review, multicase or "review of reported cases") (181)
24 22 not 23 (561)

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