

Technologies for Osteoarthritis of the Knee

An Evidence-Based Analysis

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The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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Abbreviations

OA	Osteoarthritis
NSAID	Nonsteroidal anti-inflammatory drug
QALY	Quality adjusted life year
RCT	Randomized controlled trial
TKR	Total knee replacement
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Introduction

Osteoarthritis (OA) is a chronic, degenerative, incurable disease that results in pain, joint deformity, and disability. It affects 1 in 10 adults in Ontario. More than 40% of Ontario adults aged over 60 have OA and related pain and disability. The goals of treatment are to reduce joint pain, improve joint mobility, and limit functional impairment. Current guidelines, established by the American College of Rheumatology for the Medical Management of Osteoarthritis of the Hip and Knee, (1) and by the Ontario Program for Optimal Therapeutics, (2) are based on evidence and expert opinion. They outline a complementary approach to treatment that involves nonpharmacological management (e.g., weight loss, exercise, social support, and patient education), pharmacological interventions (e.g., acetaminophen, Cox-2 specific inhibitors, nonselective nonsteroidal anti-inflammatory drugs [NSAIDs] plus misoprostol, intra-articular glucocorticoids, opioids, and topical analgesics), and surgical treatments when pharmacological management fails.

Health technology plays a relatively minor, yet vitally important, role in the treatment of this burdensome chronic disease. Fewer than 2% of individuals in Ontario who report having OA receive surgical intervention, and only 1 of 1,000 people with the disease receives the terminal intervention, joint replacement. As the recent Institute for Clinical Evaluative Sciences Research Atlas on Arthritis (3) indicates, most of the patient's encounters with the health system for management of OA occur upstream to technological interventions. It is important to frame the utilization of technology for OA of the knee within the system and sequence of care, because the appropriateness and use of treatment in the early stages of the disease have a direct impact on the need and demand for the technology downstream

Objective

To review the evidence on the effectiveness of 3 technologies to treat OA of the knee: intra-articular hylan G-F 20 (brand name Synvisc), a Class 4 device licensed by Health Canada (licence 8394) and manufactured by Genzyme Biosurgery, a division of Genzyme Corporation (Cambridge, MA, United States); lavage and debridement; and total knee replacement (TKR). Hylan G-F 20 is a hyaluronic acid derivative that is injected into the joint through a process known as viscosupplementation to manage the pain of OA. Arthroscopic lavage and debridement involves the visually guided introduction of saline solution into a knee joint and removal of fluid with or without smoothing of the bone surface, with the possible addition of more invasive procedures such as abrasion or meniscectomy (the excision of an intra-articular meniscus, as in the knee joint). Total knee replacement is a surgical procedure in which an artificial joint or prosthesis replaces a painful damaged knee joint.

Clinical epidemiologists with the Medical Advisory Secretariat systematically reviewed the evidence on the effectiveness of these 3 technologies and presented the results to the Ontario Health Technology Advisory Committee in 3 separate health technology reviews. (4-6)

Rationale for Expert Panel

Based on the evidence, the Ontario Health Technology Advisory Committee concluded that the utility of hylan G-F 20, and lavage and debridement to treat OA of the knee was questionable; yet, use of these technologies was well diffused in Ontario. In contrast, the evidence to support TKR was convincing. Given the current system strains demonstrated by the demand and long wait list for TKR, the advisability of supporting technologies for OA with uncertain utility was questionable. Acknowledging the ambiguities in the evidence, the Ontario Health Technology Advisory Committee subsequently requested that a multidisciplinary advisory panel of clinical experts with experience in using these technologies adopt a systems perspective to integrate the evidence and advise the Ontario Health Technology Advisory Committee on the appropriate use of the technologies under review.

Purpose, Membership, and Terms of Reference

The 8-person panel comprised 2 orthopedic surgeons, 2 general practitioners, 1 rheumatologist, 1 epidemiologist who was the director of the Arthritis Community Research Education Unit, and 2 physiotherapists. The purpose of the panel was to integrate the evidence and clinical expertise on viscosupplementation (i.e., hylan G-F 20), arthroscopic debridement and lavage, and TKR for the treatment of OA of the knee, and to make recommendations on the appropriate indications for and utilization of these technologies in the sequence of care of OA of the knee in Ontario. The membership and terms of reference of the panel are listed in Appendices 1 and 2, respectively.

Methods

The panel met face-to-face twice for 2 half-day sessions for 8 weeks. The first session mostly involved staff from the Medical Advisory Secretariat presenting the evidence on the effectiveness of these technologies to the panel members. The second session involved a discussion to identify the indications for which the technologies might be recommended or offered. Dr. Geoff Anderson, an expert skilled in leading such sessions, facilitated this discussion and was prepared, if necessary, to lead a RAND-Delphi exercise to identify and elaborate areas of agreement, disagreement, and uncertainty among panel members. The Rand-Delphi process involves eliciting statements about a complex issue from an expert panel, who subsequently individually score their level of agreement or disagreement with the statements through a facilitated, iterative process.

Questions Asked of the Panel

1. What is the level of evidence on the clinical utility of the technologies?
2. For what set of indications are the technologies recommended and not recommended?
3. For what set of indications might the technologies, if not recommended, be offered?
4. What is the appropriate placement of these technologies in the sequence of treatments for OA of the knee in Ontario?
5. To what extent are the technologies underused and overused in Ontario?
6. What suggestions do you have to improve the use of the technologies to optimize the management of OA in Ontario?

Definitions

For this report, the panel was asked to distinguish between the indications for which a technology is recommended and the indications for which it might be offered. Thus, in this context:

- **Recommended** implies there is strong evidence to support the clinical utility of the technology for the listed indications; whereas,
- **Offered** implies there is uncertainty and weaker evidence, but the technology may deliver more benefit than harm, although other alternatives may be equally reasonable.

Results

Each panel member contributed substantially to the discussion and the resulting report. Overall, there was general agreement among the panel members on the level of evidence of clinical utility and on the indications for which the technology might be recommended or offered; therefore, there was no need to undertake a formalized RAND Delphi exercise.

Summary of the Evidence

Hylan G-F 20

- The Medical Advisory Secretariat identified only 4 small, high-quality randomized controlled trials (RCTs) on hylan G-F 20. (7-11)
- The available evidence suggests that hylan G-F 20 reduces the pain of OA of the knee in some people between 13 and 26 weeks after receiving the injection in the early stages of the disease as an adjunct to medical management. (9)
- Most trials are short-term, and the evidence on the effectiveness of repeat treatment cycles is limited.
- Hylan G-F 20 is not effective for people with advanced disease. (8)
- The magnitude of pain relief delivered by hylan G-F 20 is small, comparable to intra-articular steroids and NSAIDs. (5)
- Hylan G-F 20 carries a risk of a severe, inflammatory reaction. This has been reported in 31 out of an estimated 15,000 cases treated with hylan G-F 20. This figure is based on the Canadian Adverse Drug Reaction Monitoring Program (12) and may be an underestimate. It is not clear which patients may be at higher risk.

Lavage and Debridement

- Evidence on lavage and debridement is limited. Using Medical Advisory Secretariat-defined inclusion/exclusion criteria, 3 RCTs (11;13;14) and 2 large case series (15;16) were identified, , along with 5 smaller case series (17-21)
- The results of 1 RCT (11) (N = 90) of patients with early-stage OA demonstrated that lavage did not result in a clinically relevant improvement in joint pain nor joint function at 12 months after the procedure.
- Another RCT (13) (N = 180) of patients with advanced OA indicated that neither lavage alone nor debridement (meniscal tears on magnetic resonance imaging excluded) was effective at improving pain and function up to 24 months following the procedure.
- A small RCT (14) (N = 76) of patients with OA localized to a degenerative lesion in the medial femoral condyle (a rounded projection on a bone) reported debridement was effective at reducing pain for up to 5 years.
- The results of 5 case series (15;16;19-21) of patients who had arthroscopic debridement (with meniscectomy, as appropriate) suggest that the set of surgeries may be effective in those with unicompartmental disease (especially the medial), shorter symptom duration, sudden onset of mechanical symptoms, a recent meniscal tear, preoperative full range of motion, and early-stage OA.
- However, as the results from these case series are derived from poor quality evidence, identifying subsets of patients that may benefit from this procedure requires further testing. Furthermore, the effectiveness of meniscal repair (relative to no repair) can be answered only in an RCT.

Total Knee Replacement

- Data from the Ontario Joint Replacement Registry (Personal Communication, July 2005) indicate 80% of people who have TKRs have near-normal (> 88) Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)¹ (22) scores 1 year after procedure, and 84% of patients report being either satisfied (25%) or very satisfied (59%) with the outcome.
- In patients with lower preoperative physical function, function and pain did not improve postoperatively to the level achieved by those with higher preoperative function. (23) Data from the Ontario Joint Replacement Registry suggest conventional Ontario practice is to defer knee surgery until pain and function is relatively severe despite medical management.
- There is anecdotal evidence that one reason for deferral is surgeons' reluctance to perform TKR in relatively young patients that may outlive the device and thus would require a revision.
- Data from the Swedish Joint Registry (24) indicates that people who received joint replacements between 1988 and 1992 had a revision rate of about 8% after 10 years, and that this rate has steadily declined over the years. This steady decline could be related to improvement in the quality of device and surgical techniques.

Expert Panel Review

Answers to the Questions Asked

1. What is the level of evidence on the clinical utility of the individual technologies?

Overall, the panel agreed on the following points:

- There is good, consistent evidence that TKR is effective for patients with moderate to severe OA of the knee.
- The evidence on lavage alone is limited and does not demonstrate that it has clinically significant utility.
- The evidence on debridement is sparse and inconsistent. Debridement may have some clinical utility in patients with mild to moderate OA and mechanical symptoms, but this evidence is indirect and of poor quality. There was concern over the lack of a standard acceptable definition of debridement and uncertainty about the role aggressive debridement may play in accelerating OA.
- There is some evidence than hylan G-F 20 has some utility as an adjunct for patients with persistent pain and mild disease, despite optimal primary care. However, the magnitude of effect is relatively small, producing pain relief for 13 to 26 weeks on a magnitude equivalent to intra-articular steroids and NSAIDs. The cost of hylan G-F 20 relative to intra-articular steroids makes the latter the preferred option.
- Part of the challenge in interpreting the evidence is because there is little evidence on the natural history of OA.

2. For what set of indications are the technologies recommended and not recommended? For what set of indications might the technologies, if not recommended, be offered?

Recommended: Total knee replacement

¹ The WOMAC is the most widely used and best-proven condition-specific health assessment instrument for patients with OA of the lower extremities. It has 24 items that measure 5 dimensions of pain, 2 of stiffness, and 17 of physical function. The scales for each dimension may be ordinal, based on a Likert scale (0–4) scale ranging from 0 (“no symptoms”) to 4 (“extreme symptoms”), or continuous, using a visual analogue scale. It can be scored in a number of ways, including the total sum out of 96, or by the mean ordinal or continuous score for each item or dimension.

The panel concluded that there was sufficient evidence to recommend TKR for patients with all of the following characteristics:

- Radiographic evidence of moderate to severe disease
- Individual has had a trial of optimal primary care management
- Persistent, moderate to severe pain resulting in limited function despite optimal primary care management
- WOMAC scores indicate significant pain and disability
- Disease status presents threat to social role and quality of life
- No absolute contraindication to TKR (note, neither age or increased BMI are absolute contraindications to surgery)
- Informed and accepting of risk of surgery, and need for postoperative rehabilitation and likelihood of revision

Contraindications to TKR Surgery (any of the below):

- Contraindications specific to TKR: No neuromuscular function of the quadriceps or joint infection
- Contraindications related to operative risk: Risk due to pre-existing medical conditions

Offered: Debridement

The panel concluded there is insufficient evidence to recommend debridement, but that it might be offered to people who meet all of these criteria:

- Unwilling to have TKR
- Pain not overwhelming
- Radiographic imaging suggests mild to moderate disease (< 50% loss of articular joint space)
- Mechanical symptoms
- Magnetic resonance imaging confirms mechanical etiology (i.e., evidence of meniscal tear)

Contraindications to debridement:

- Patient has no mechanical signs (e.g., clinical picture consistent with patellofemoral syndrome, negative magnetic resonance imaging scan)

The uncertainty derives not only from the paucity of the evidence, but also because orthopedic surgeons do not have a standard way of describing and categorizing the pathology of OA of the knee. Moreover, there is no standard acceptable definition of debridement. There is some concern that aggressive debridement may accelerate the progression of the disease, although most of the available evidence is short term and fails to capture long-term effects. Occasionally, arthroscopic investigation may contribute to the diagnosis of OA; however, the panel agreed that in most cases arthroscopy was not required to diagnose OA and it should not be considered to be or used as primarily a diagnostic modality for OA.

Lavage

The panel felt there was no evidence to support the utility of lavage alone for the treatment of OA, although it may have utility for indications other than OA.

Offered: Hylan G-F 20

The panel thought that the quality of evidence for hylan G-F 20 was poor, and that there was uncertainty

about the magnitude of clinical benefit produced by hylan G-F 20 and the risk it carries of a severe adverse event (inflammatory arthrosis). Accordingly, the panel thought that hylan G-F 20 should not be part of routine care for OA. There was disagreement among the panel, however, with some members feeling that it should not be offered, and others feeling that it might be offered given the following indications/in these situations:

- In early disease as an adjunct to medical management (equivalent to intra-articular steroids and NSAIDs).
- One course could be offered to patients who have failed optimal primary care management, including steroids (not recommended as routine care).
- Could be offered to individuals who are unwilling to have a surgical assessment and who do not meet the objective criteria for TKR.

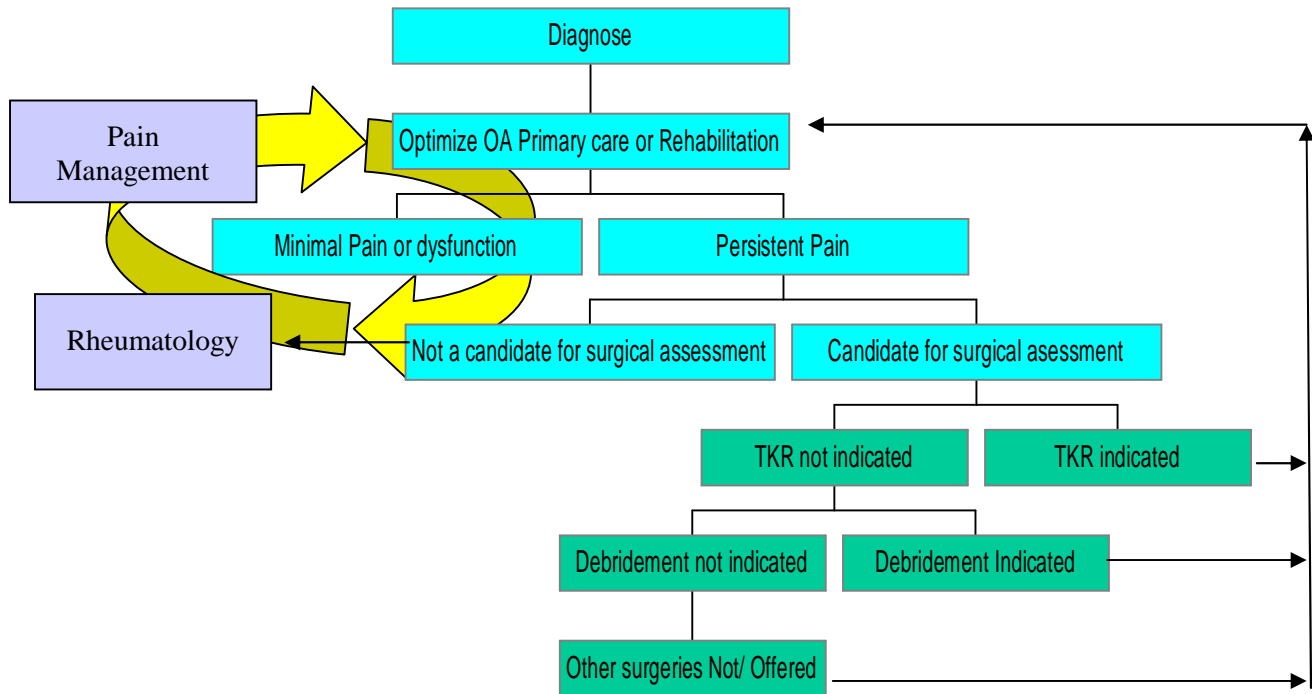
Contraindications to hylan G-F 20:

- Advanced disease (i.e., meets eligibility for knee replacement or on the waiting list for TKR)

3. What is the appropriate placement of these technologies in the sequence of treatments for osteoarthritis of the knee in Ontario?

To indicate when, along the care pathway, these technologies might be recommended or offered, the panel thought it was important first to outline the appropriate sequence of care for OA (Figure 1).

Figure 1: Treatment Pathway for Osteoarthritis



Steps along the pathway:

1. Start with the correct diagnosis (not all knee pain is OA).
2. Ensure the patient has a trial of optimal primary care prior to referral for orthopedic assessment. The components of optimal primary care are shown in Table 1 and include referral to the Arthritis Society of Canada.
3. If pain persists, determine whether the patient is a candidate for surgical assessment (Table 2).
4. If the patient is unwilling to consider surgery, ensure he or she returns to the expanding circle of care, which may involve rheumatologists and pain specialists, and the multidisciplinary primary care team.
5. If the patient is willing to consider surgery, refer her or him to an orthopedic surgeon for surgical assessment.
6. The orthopedic surgeon should first consider whether the patient has all the indications for which TKR is recommended and, if so, the patient should have TKR, followed by rehabilitation and then return to the multidisciplinary primary health care team.
7. If the patient does not have the indications for TKR, debridement might be offered if the patient has all the indications.
8. Otherwise, other surgeries might be offered.
9. In all cases, the patient returns to multidisciplinary primary care,

Within this sequence, TKR is recommended at step 6. Hylan G-F 20 may be offered at step 4. Debridement may be offered at step 7.

Table 1: Components of Optimal Primary Care

➤ Appropriate diagnosis

- Analgesics (May include trial of narcotics, intra-articular injections)
- Exercise/physiotherapy to recondition muscles
- Weight loss prn (i.e., as needed/directed to by physician)
- Patient self-management program
- Home assessment
- Assistive devices prn (i.e., as needed/directed to by physician)
- Patient education including discussion of surgical options
- Referral to the Arthritis Society of Canada

Table 2: Criteria for Referral for Surgical Assessment

- Persistent pain and/or threat to role function despite trial of optimal primary care
- Patient willing to consider surgery
- No absolute contraindications to total knee replacement (see below for list of absolute contraindications)
- Note: Neither age nor body mass index are contraindications to referral for surgical assessment

In building this pathway, the panel emphasized the following points:

- Recognize the foremost importance of optimizing multidisciplinary primary care.
- Distinguish the roles of the primary care team and specialists.
- Place the responsibility to assess suitability for referral for surgical assessment with the multidisciplinary primary care team.
- The objective of care is to avoid the potential terminal problem of OA, which is one of chronic pain and disability once surgical options have been exhausted.
- Position TKR as one of the first surgical options to be considered.
- Depict the iterative cycle of care for this chronic and potentially progressive disease.
- Acknowledge the availability of other surgical techniques not reviewed in this exercise (for which evidence is limited).

4. To what extent are the individual technologies underused and overused in Ontario?

Total knee replacement: underused

The panel pointed out that it is important to distinguish between need and demand for TKR, given that patient preference plays a huge role in the demand for TKR in Ontario. According to a recent cross-sectional study (25), about 4% to 5% of the general population aged over 55 years needs TKR (based on a WOMAC score > 39/100, and clinical and x-ray evidence of OA). About 20% of these have contraindications to TKR. Thus, excluding these patients, the data suggest that the estimated need for TKR is 2.9% to 3.6% of the general Ontario population aged over 55 years. However, only about 25% to 30% of those who need TKR are probably or definitely willing to receive it. There are approximately 2.7 million people aged 55 years and over in Ontario, based on 2001 estimates. According to these figures, the number of TKRs (circa 11,000 per annum) delivered in Ontario fails to meet the demand, never mind the need for this effective surgery.

Table 3: Need, Demand and Supply: Total Knee Replacement in Ontario

Total Knee Replacement	Proportion of Population 55+	Absolute Numbers
Need	3.25	86,773
Demand	0.9	24,029
Current supply	0.4	11,000
Shortfall (demand)	0.5	13,029
Shortfall (need)	2.75	75,773

Unpublished data from the Ontario Joint Registry suggest that people with OA in Ontario are receiving TKR at a relatively advanced stage in their disease (Personal communication, July 2005). According to data from the Ontario joint registry, (Personal communication, July 2005) the mean baseline WOMAC scores for function and pain among joint replacement recipients in Ontario were 40 and 11, respectively, yet there is evidence that people with higher baseline function and less pain (i.e., WOMAC scores of 25 and 8, respectively) who receive the replacement have better outcomes. (23;26)

Several factors contribute to the underuse of TKR in Ontario. The 3 main ones identified by the panel are:

- There is patient misperception and misinformation about the risks and benefits of TKR. (20)
- In routine practice, physicians do not fully understand the indications for, and risks and benefit of, TKR. (27)
- There is limited capacity for and inappropriate utilization of orthopedic surgical time. According to a recent survey, (27) orthopedic surgeons spend about two-thirds of their clinical time seeing patients in the office instead of in the operating room. Some of this time is spent optimizing the medical management of patients referred for surgical assessment too early in their care, and some is spent with patients who are either unwilling to consider TKR, or who for whom TKR is not recommended.

Debridement: overused

The lack of a standard definition of debridement and a standard way of describing and categorizing the pathology of OA of the knee present methodological challenges that make it difficult to identify the extent to which debridement is being overused in Ontario. The panel agreed that debridement is inappropriate and should not be used for someone who is scheduled for knee surgery.

In 2002, Wai et al (28) presented the results of their analysis of hospital utilization data, which suggested that about 9% of people who received arthroscopic surgery between 1992 and 1996 in Ontario proceeded to a TKR within a year of arthroscopy. These results are consistent with an analysis of a more recent (2002–2003) dataset of Ontario fee schedule codes R204, 205, 206, 289, 441, 482, 483; and OHIP Dx code 715 (OA). Based on these data, about 12% of people who received debridement in 2002 received a TKR by the end of 2003, amounting to between 441 and 546 TKRs. Although the limitations of these data must be acknowledged – for example, it is not known whether the debridement and TKR occurred on the same knee – this pattern does suggest that arthroscopic debridement is overused among patients who would likely fare better with a TKR.

Lavage: status quo

Only about 50 lavage-alone (compared with lavage and debridement) procedures are conducted in Ontario per year. The panel felt this low utilization rate was appropriate, given that the effectiveness of lavage alone for treating OA is uncertain and not supported by sufficient evidence.

Hylan G-F 20: status quo

According to the volume of sales of hylan G-F 20, only about 3,500 people in Ontario receive hylan G-F 20 per year. This is a small proportion (< 1/100) of the more than 350,000 people that seek medical attention for OA of the knee annually. According to the panel, this low utilization rate is appropriate; moreover, they concluded that expanded use of hylan G-F 20 should not be supported by the Ministry of Health and Long-Term Care because the magnitude of benefit of this technology is relatively small and outweighed by its high cost and uncertain adverse event profile.

5. What suggestions do you have to improve the use of the technologies to optimize the management of OA in Ontario?

In response to this question, the panel offered the following suggestions:

- Improve the primary care of OA and reduce the need for TKR. Possible mechanisms to achieve this include exploring different models of delivering primary care, (29) developing a practice guideline on the essential components of optimal primary care, and reducing barriers to delivering effective preventive care (e.g., the OHIP billing restrictions on family physicians and limited access to physiotherapy).
- Increase the capacity for joint replacement by making surgeons more available. Possible mechanisms to achieve this include developing a practice guideline for primary care physicians describing the indications for appropriate referral to orthopedic surgeons for surgical assessment, discouraging overuse of arthroscopic debridement through clinical practice guidelines, and perhaps auditing hospital records.
- Address the unmet need for TKR. Mechanisms to achieve this include developing a patient education campaign to dispel misperceptions and educate patients about the about the risks and benefits of TKR.
- Educate physicians about the risks and benefits of TKR. Mechanisms to do this include developing and disseminating a clinical practice guideline to on the appropriate indications for TKR, debridement and viscosupplementation.
- Encourage standard criteria for the categorization of OA pathology and definition of debridement. Mechanisms to do this include developing and disseminating a clinical practice guideline targeted at orthopedic surgeons.

Economic Analysis

Notes and Disclaimer

The Medical Advisory Secretariat uses a standardized costing methodology for all of its economic analysis of technologies. The main cost categories and the associated methodology from the province's perspective are as follows:

Hospital: Ontario Case Costing Initiative (OCCI) cost data is used for all program costs when there are ten or more hospital separations or one-third or more of hospital separations in the ministry's data warehouse are for the designated ICD-10 diagnosis and CCI procedure codes. Where appropriate, costs are adjusted for both hospital specific or peer-specific effects. In cases where the technology under review falls outside the hospitals that report to the OCCI, PAC-10 weights converted into monetary units are utilized. Adjustments may need to be made to ensure that the relevant Case Mix Group is reflective of the diagnosis and procedures under consideration. Due to the difficulties of estimating indirect costs in hospitals associated with a particular diagnosis/procedure, the MAS normally defaults to considering direct treatment costs only.

Historical costs have been adjusted upward by 3% per annum representing a 5% inflation rate assumption less a 2%

implicit expectation of efficiency gains by hospitals. Non-Hospital: These include physician services costs obtained from the Provider Services Branch of the Ontario Ministry of Health and Long Term Care, device costs from the perspective of local health care institutions and pharmaceutical costs from the Ontario Drug Benefit formulary list price. Discounting: For all cost-effective analysis, discount rates of 5% and 3% are used as per the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) and the Washington Panel of Cost-Effectiveness, respectively. Downstream cost savings: All cost avoidance and cost savings are based on assumptions of utilization, care patterns, funding and other factors. These may or may not be realized by the system or individual institutions.

In cases where a deviation from this standard is used, an explanation has been given as to the reasons, the assumptions and the revised approach.

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

ICD-10: (International Classification of Diseases)
CCI: Canadian Classification of Health Interventions

Cost-Effectiveness Analysis

A cost-effectiveness/utility analysis was conducted for 2 subsets of patients. In subset A (older patients), costs and quality adjusted life years (QALYs) were determined for a patient originally slated to have surgery at age 70 but who had the operation 5 years earlier, at age 65. In subset B (younger patients), costs and QALYs were determined for a patient originally slated to have TKR at age 65 but who had the surgery 5 years earlier, at age 60.

Incremental costs and QALYs were calculated and discounted to the present for the remaining life expectancy of each patient. In each case, a female patient is analyzed with a life expectancy of 82.2 years; for a male patient, the life expectancy is 77.7 years. The device is assumed to last 15 years on average for older patients and 10 years for younger patients.

Utilities were obtained from studies on the cost-effectiveness of various treatments for total hip replacement that was compiled by the Harvard Center for Risk Analysis. (30) This article mapped utilities to the 4 functional classes of the American College of Rheumatology (Table 4). The functional classes for hip OA were used as proxies for knee OA because of our assumption that the experiences of both sets of patients with regard to life-limiting events should be similar.

The preoperative stage used was ACR Class 3 (with an associated utility of 0.5) for the analysis and the patient returns to stage 1 (for younger patients) and stage 2 (for older patients) post surgery. This was based on input from the OA Expert Panel. It is also assumed in this case that only a single joint was involved and there were no musculoskeletal comorbid conditions.

Table 4: Functional Classes of Osteoarthritis of the Hip*

Utility**	ACR Class	Description
1	1	Complete ability to carry on all usual duties without handicaps
0.8	2	Adequate for normal activities despite handicap of discomfort or limited motion of hip

0.5	3	Limited only to little or none of duties of usual occupation or self-care
0.3	4	Incapacitated, largely or wholly bedridden, or confined to wheelchair; little or no self-care

*American College of Rheumatology (<http://www.rheumatology.org>)

** JAMA, A cost-effectiveness analysis of total hip arthroplasty for OA of the hip).

Note that for cost analysis, the following components were taken into account: the cost of a single TKR is \$10,375 which includes hospital costs, physician costs, medication costs and follow-up consultations; the cost of rehabilitation after surgery is \$1,500 for one year. All costs are conservative and based on minimal usage. The cost of surgery has been adjusted for inflation.

For subset A, the analysis shows that undertaking TKR 5 years sooner, at 65 instead of 70 years, increases the number of QALYs and produces a general decrease in costs over the original therapeutic trajectory. The proposed process dominates over the current approach producing lower costs and more QALYs.

Table 5: Cost of Having a Total Knee Replacement Five Years Sooner in Older Patients*

	Current	Proposed†
Cost, Cdn	26,000–30,000	23,000–27,000
Quality adjusted life years, number	8.4–10.0	9.8–11.3

*Subset A: at 65 instead of 70 years of age.

†The proposed model dominates.

For subset B, the analysis show that undertaking TKR five years earlier from age 65 to age 60 increases the number of QALYs and minimally increases the cost. The proposed approach has a highly favourable cost-effective ratio that ranges from \$2,905–\$3,373 per QALY.

Table 6: Cost of Having a Total Knee Replacement Five Years Sooner in Younger Patients *

	Current	Proposed
Cost, Cdn	36,000–43,000	38,000–45,000
Quality adjusted life years, number	9.7–11.9	10.5– 12.5

*Subset B: at 60 instead of 65 years of age.

In both subset analyses, bringing TKR forward is either a cost-saving strategy or a very favourable, cost-effective strategy.

Budget Impact Analysis

The weighted mean cost (in academic/community hospitals) for TKR is \$8,767 (Cdn). Together with medication, follow-up consultation, and OHIP costs, the total estimated cost for TKR is \$10,375

(2004/2005 figures; Cdn). In 2003/2004, 12,933 TKRs were done; the estimate for 2005/2006 is 17,173.

The budget impact analysis was conducted based on the following assumptions: TKR supply increases by 14% over the next 3 years and then remains constant, and total costs incurred start at \$204 million (Cdn) annually and rise to \$351 million (Cdn) by 2010. This is based on the inflation-adjusted total cost of surgery multiplied by the projected number of surgeries. Cost avoidance is based on the reduction in the number of inappropriate debridement procedures with the onset of better clinical guidelines as proposed by the OA Expert Panel. A conservative estimate is that 10% of these debridement procedures are inappropriate and thus avoidable. The downstream savings impact caused by the reduction in inappropriate debridement can be recognized beginning in 2007 assuming the new guidelines for treatment of OA is adhered to by practitioners. The current cost of each debridement is about \$1,100 (Cdn). Other costs that can be avoided by undergoing TKR include fewer physician visits (estimated reduction by 50%) and analgesics (cost savings of around \$1,100 annually). Cost avoidance, as such, could potentially rise from \$35 million to \$174 million (Cdn) in the first 5-year period.

Recommendations

1. TKR is recommended for people who meet the indications specified by the panel. The need for TKR is much greater than current demand or capacity. Efforts should be made to improve access to TKR through a patient education campaign to dispel misinformation, clinical practice guidelines targeted at primary care physicians, a revised model of delivering primary care that encompasses multidisciplinary primary care teams, and an efficient system of referral so that orthopedic surgical time is used more efficiently.
2. Debridement is not recommended for the treatment of OA, but may be offered to people who meet the limited indications. Efforts should be made to standardize the definition of debridement and categorize the pathology of OA in the knee, and to discourage overuse of debridement by means of clinical practice guidelines, audits, and improved access to TKR.
3. Hylan G-F 20 is not recommended. There was disagreement among panel members. Some thought it should not be offered; others thought that it should be offered to people who have failed optimized primary care including intra-articular steroids. The conclusion was that hylan G-F 20 is not cost-effective and should not be offered as routine care.
4. The burden of chronic OA is enormous. A comprehensive strategy is needed to address the systemic problems that hamper the efficient delivery and appropriate use of technologies to treat this disease.

Appendices

Appendix 1: Expert Panel Membership List

Members

- Elizabeth Badley, Ph.D., Head, Division of Outcomes and Population Health, and Director, The Arthritis Community Research and Evaluation Unit, Toronto Western Hospital Research Institute
- Aileen Davis, Ph.D., Senior Scientist, Toronto Rehabilitation Institute, Associate Professor, University of Toronto
- Allan E. Gross, MD, FRCSC, Orthopedic Surgeon, Mount Sinai Hospital
- Gillian Hawker, MD, Internal Medicine, Women's College Hospital
- Gwen Jansz, MD, St. Jamestown Health Centre
- Robert Lam, MD, MSc, CCFP, FCFP, Associate Professor, University of Toronto, University Health Network
- Crystal MacKay, MHSc, BScPT, Research Associate, Arthritis Community Research and Evaluation Unit
- Nizar N. Mahomed, MD, ScD, Associate Professor, Department of Surgery, Director, Musculoskeletal Health and Arthritis Program, University Health Network

Ex officio members

- Ruth Carlisle, Policy Analyst, Population Health Policy & Planning & Women's Health Branch, Integrated Policy & Planning Division, Ministry of Health and Long-Term Care
- Mayvis Rebeira, Senior Project Consultant, Health Results Team, Ministry of Health and Long-Term Care
- Erica Weir, Clinical Epidemiologist, Medical Advisory Secretariat, Ministry of Health and Long-Term Care
- Graham Woodward, Manager, Health Information Products & Services Unit, Knowledge Management & Reporting Branch, Integrated Policy & Planning Division, Ministry of Health and Long-Term Care
- Geoff Anderson, RAND-Delphi process
- Waseem Sharieff, decision analyst and clinical epidemiologist, Medical Advisory Secretariat, Ministry of Health and Long-Term Care

Appendix 2: Expert Panel Terms of Reference

Objective

The aims of this analysis were as follows:

- To review and consolidate evidence on the clinical utility of technologies for the treatment of osteoarthritis (OA) of the knee
- To answer specific question posed by the Ontario Health Technology Advisory Committee
- To recommend appropriate indications and allocations of resources to use these technologies in Ontario
- To provide a written report of the recommendations to the Ontario Health Technology Advisory Committee

Reporting of Committee Products

The committee will report through the Medical Advisory Secretariat to the Ontario Health Technology Advisory Committee.

Timeframe and Process

The panel's recommendations will be submitted to the Medical Advisory Secretariat no later than November 2005. The process will involve (see Appendix 4) a review of the available evidence; an accepted, facilitated method of assessing clinical utility and appropriateness; consideration of the burden of the disease; need for the technology; and resource implications. Panelists will be expected to read background materials, complete some structured questionnaires (see Appendix 5); and attend 3 (or so) half-day meetings (expected in July–October).

Expenses

The Ministry of Health and Long-Term Care will assume responsibility for travel expenses incurred by meeting participants.

Scope of the Review

- Effectiveness of technologies used in treating OA of the knee (intra-articular hyalan G-F 20, arthroscopic debridement and lavage, total knee replacement)
- Indications for appropriate use of 1 or more of these technologies
- Assessment of burden of illness and need/demand for these technologies
- Cost and resource implications of using these technologies in sequence or alone in specific types of patients, over the course of disease progression

Deliverable

The deliverable is a written report of the integrated evidence that includes recommendations for clinical guidelines on appropriate use of these technologies and assessment of the resource implications to maximize clinical utility of these technologies under the realistic limitations of resource constraints.

Support of the Medical Advisory Secretariat

The Medical Advisory Secretariat will conduct a systematic health technology and policy analysis for each of the technologies under consideration. The health technology and policy analyses will be provided to the expert advisory panel and will serve as the basis for the panel's analysis.

Guiding Principles

- The panel's advice will be predicated on evidence-based analyses of effectiveness, consideration of economic and societal implications, and other determinants as deemed appropriate (Appendix 6) by the members. The advice will be based on processes that are objective and transparent.
- The levels of evidence and GRADE of recommendations used by the Medical Advisory Secretariat in its health technology assessments can be found in Appendix 7.

Conflict of Interest and Confidentiality

- Panel members must ensure that any actual or potential conflict of interest arising in regard to any matter under discussion by the panel is drawn to the attention of the chair. The chair will determine what action, if any, is required arising from the conflict of interest and will take appropriate action.
- Members may not use any data or information obtained as a result of their membership on the panel for their personal financial benefit or gain, or for the benefit or gain of any entity or corporation in which they have a financial interest or in which they have an interest as an employee or officer.
- All information and material of any kind whatsoever acquired or prepared by or for the panel shall, both during and following the duration of this panel, be the sole property of Her Majesty the Queen in right of Ontario as represented by the Minister of Health and Long-Term Care.
- Members undertake to keep confidential and inviolate and not directly or indirectly disclose to any person, association of persons, corporations or government, or use at any time, either during or subsequent to their term as a member of the panel, any data or information that is not generally available to the public during the deliberations of the panel and during the 60 days following the Ontario Health Technology Advisory Committee making any recommendation relating to the work of the panel.
- Publications resulting from the panel's work will be permitted as long as the Ministry of Health and Long-Term Care has been given the opportunity to review the publication 30 days prior to submission for publication and that publication is not released during the 60-day period following the Ontario Health Technology Advisory Committee reaching and delivering a recommendation to the ministry.
- Members are requested to refer media inquiries about the panel and its work to the chair.

Appendix 3: Proposed Work Plan

Proposed work plan to integrate Medical Advisory Secretariat (MAS) health technology and policy assessments (HTPA's) on technologies for treatment of osteoarthritis (OA) of the knee

Background

In February 2005 OHTAC prioritized 3 technologies for treatment of osteoarthritis of the knee to undergo assessment of their effectiveness and consequential Ontario health policy implications. These were intra-articular hylan, arthroscopic debridement and total knee replacement. The results of the individual health technology and policy analyses (HTPAs) were presented to OHTAC in June, 2005. On reviewing the evidence, OHTAC recommended that a provincial panel of clinical experts be struck to answer specific questions arising from the evidence, to integrate the evidence and to provide recommendations to OHTAC on the appropriate utilization of these technologies in Ontario.

Objective

The primary objective of the exercise to integrate the HTPAs is to provide expert advice on which technologies (among hylan, arthroscopic surgery and knee replacement) are appropriate for which patients (age and stage of disease). The decisions will be based on the evidence of the magnitude and duration of clinical benefit (mostly pain relief) from the technology, cost, opportunity cost (of not pursuing an alternative treatment arm) and rate of disease progression over the natural history of the illness as best as we can understand it.

Method

The exercise will involve four distinct phases:

1. Identifying appropriate use of technology for specific patient populations using advisory panel and RAND – Delphi technique
2. Estimating the burden and need in Ontario using data available to the MOHLTC Knowledge Management and Reporting Branch.
3. Costing out the resource implications of appropriate care
4. Recommendations to OHTAC for appropriate clinical practice and resource allocation

Phase 1. Identifying appropriate use of technology for specific patient populations

The advisory panel will be presented with the evidence on the effectiveness of the three health technologies assessed by MAS. The Panel will have the option of undertaking a RAND-Delphi technique to identify the clinical indications and utility of these technologies. This would involve identifying various clinical scenarios that portray different clinical indications for the technologies. Individually the members will rate the clinical utility of the various technologies in each scenario and areas of agreement and disagreement among panel members will be reviewed and discussed. Each member will subsequently rescore the utility of the technology in the particular scenario in consideration of this new information. The results of this exercise in Phase 1 will set the groundwork for clinical practice guidelines on the appropriate utilization of the technologies.

Phase 2. Estimating the burden.

Data available to the Knowledge management and Reporting Branch will be used to generate estimates, based on sociodemographic measures, of the number of Ontario residents who are experiencing the clinical scenarios and need for the technologies indicated in phase 1 of the exercise.

Phase 3. Costing out the resource implications of appropriate care

Once the indications for the appropriate use of the technology have been identified and the magnitude of need for the technology estimated, the cost of meeting this need appropriately will be estimated under different assumptions (i.e. limited resources, prioritizing spending and use of technology to maximize utility)

Phase 4. Recommendations to OHTAC for appropriate clinical practice and resource allocation.

The panel will advise OHTAC on the appropriate use of these technologies and the resource allocation implications.

Proposed Schedule:

September

Preliminary panel meeting to discuss method, establish panel membership, define clinical indications

Construction of clinical vignettes

Start to estimate burden of need based on patient characteristics in clinical scenarios

Completion and circulation of evidence of effectiveness (completed HTPAs), clinical scenarios, survey of appropriateness/utility of the technologies

October

Second panel meeting to review and discuss peer assessment of indications/utility and rescore indications with high extent of disagreement

If deemed helpful, construction of a decision analysis model that lays out alternate options for use of technology will be initiated

Third panel meeting to review model of burden of disease, decision analysis model and costing analysis

Final panel meeting to draft recommendations for OHTAC

Appendix 4: Examples of Clinical Indications and Scores

Clinical factors that might be considered indications for use of a specific technology to treat osteoarthritis of the knee include: age, WOMAC score, tolerance for NSAIDs, comorbid conditions, duration of disease, radiographic grade, etc.

Example of questionnaire

Appropriateness of arthroscopic debridement in an NSAID intolerant patient with no co-morbidities who will not consider knee replacement who has had OA for 4 years and for whom you are managing over a 10-year period.

A. WOMAC VAS pain score	Age 55-65 Years	Age 65-75 years
1) 0-39	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
2) 40-70	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9
3) >70	1 2 3 4 5 6 7 8 9	1 2 3 4 5 6 7 8 9

Appropriateness scale 1=extremely inappropriate, 5=uncertain, 9=extremely appropriate

Appendix 5: Examples of Potential Treatment Pathways

Sketch of possible competing treatment options over 10 years that might feed into decision and costing analysis

Relative Cost

Options

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
1	Hylan -----									
2	Art Deb ++++++					Art Deb ++++++				
3	TKR *****									
4	Hylan -----		Art Deb ++++++			TKR *****				
5	Hylan -----			Art Deb ++++++			Art Deb ++++++			
6	Hylan -----		TKR *****							
7	Art Deb ++++++			TKR *****						

Art Deb = arthroscopic debridement

TKR = total knee replacement

Appendix 6: Levels of Evidence and GRADE of recommendations Used in MAS' Health Technology Policy Assessments

Study Design	Level of Evidence
Large RCT, systematic reviews of RCTs*	1
Large RCT unpublished, but reported to an international scientific meeting	1(g)
Small RCT	2
Small RCT unpublished, but reported to an international scientific meeting	2(g)
Non-RCT with contemporaneous controls	3a
Non-RCT with historical controls	3b
Non-RCT presented at international conference	3(g)
Surveillance (database or register)	4a
Case series with more than 2 years of follow-up (multi-sites)	4b
Case series with less than 2 years of follow-up	4c
Retrospective review, modelling	4d
Case series presented at international conference	4(g)

g=grey literature

*RCT represents randomized controlled study.

GRADE approach

The GRADE approach permits consideration of 4 key elements: study design, study quality, level of consistency in estimate of effects across studies and extent of directness (i.e. the extent to which the people, interventions and outcome measures are similar to those of interest). The GRADE scoring process assigns an initial score (any of high, moderate, low, very low) according to the type of design (i.e. "high" for randomized trials, "low" score observational studies and "very low" for any other evidence).

Indications to decrease the grade include: serious (-1) or very serious (-2) limitations to study quality, important inconsistency in the direction and magnitude of effect across studies (-1), some (-1) or major (-2) uncertainty about directness, imprecise or sparse data (-1), and high probability of reporting bias (-1).

Indications to increase the grade include: strong evidence of association (i.e. significant relative risk >2.0 based on consistent evidence from two or more observational studies with no plausible confounders (+1), very strong evidence of association (i.e. RR>5), evidence of a dose-response gradient (+1) or (+1) if all plausible confounders that would have reduced the effect are accounted for. When studies are downgraded on the basis of quality concerns, reviewers must make explicit their reasons.

Once the quality of the evidence has been assessed, the relative magnitude and certainty of the effect is balanced against the level and certainty of risk and burden. If the benefit clearly outweighs the risk and burden with certainty, then a strong recommendation can be made on the basis of the evidence. On the other hand, if the benefit does not outweigh the risk and burden or if there is uncertainty about these benefit, risk or burden, then the strength of the recommendation is weaker.

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