ROBOT-ASSISTED KNEE ARTHROPLASTY

Effectiveness and cost-effectiveness of robot-assisted primary knee replacement in the published literature and implications for British Columbia.

HEALTH TECHNOLOGY ASSESSMENT REPORT

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All inferences, opinions, and conclusions drawn in this publication are those of the authors, and do not necessarily reflect the opinions or policies of the British Columbia Ministry of Health, or any individual stakeholders involved in this project.

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List of Abbreviations

2D	Two Dimensional
3D	Three Dimensional
BC	British Columbia
bi-UKR	Bi-Unicompartmental Knee Replacement
BMI	Body Mass Index
CADTH	Canadian Agency for Drugs and Technologies in Health
CIHI	Canadian Institute for Health Information
CJRR	Canadian Joint Replacement Registry
CT-scan	Computed tomography scan
DAD	Discharge Abstract Database
EDSP	Evidence Decision Support Program (AB)
HR	Hazard Ratio
HTA	Health Technology Assessment
HTAO	Health Technology Assessment Office
ICD	International Classification of Diseases
ICER	Incremental Cost-Effectiveness Ratio
ICUR	Incremental Cost-utility Ratio
LOS	Length of Stay
MDRD	Medical Device Reprocessing Department
MRI	Magnetic Resonance Imaging
NA	Not Available/Not Reported
NHS	National Health Services
NNT	Number Needed to Treat
OA	Osteoarthritis
OR	Odds Ratio
OR	Operating Room
P	P-value
PHSA	Provincial Health Services Authority
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-Adjusted Life-year
r-biUKR	Robot-assisted Bi-Unicompartmental Knee Replacement
RCT	Randomized Controlled Trials
RD	Risk Difference
RFP	Request for Proposal

RN	Registered Nurses
ROM	Range of Motion
RR	Risk Ratio
r-TKR	Robot-assisted Total Knee Replacement
r-UKR	Robot-assisted Unicompartmental Knee Replacement
S&N	Smith & Nephew
SD	Standard Deviation
TKR or cTKR	Conventional Total Knee Replacement
UK	United Kingdom
UKR or cUKR	Conventional Unicompartmental Knee Replacement
USA	United States of America
USB	Universal Serial Bus
VAT	Value of Analysis Team
VCH	Vancouver Coastal Health Authority
WMD	Weighted Mean Difference
CI	Confidence Interval
EQ5D	EuroQol Five-dimension Scale Questionnaire
FHA	Fraser Health Authority
FNHA	First Nation Health Authority

Executive Summary

Background:

Osteoarthritis (OA) of the knee is a chronic degenerative disease, resulting in pain, loss of function and instability of the knee. It leads to reduced quality of life, and is associated in general with a higher risk of mortality. Knee OA is very common among individuals aged 40 years and older with an estimated prevalence of 15.8% (approximately 440,000 individuals ≥ 40 years in British Columbia).

Treatment goals for knee OA include symptom relief and preservation of joint function to improve quality of life and maintain activity levels. Treatment options include conservative treatment (e.g., physiotherapy), pharmacological treatment (e.g., pain medication such as non-steroidal anti-inflammatories, and corticosteroid injections) and surgery (e.g., knee arthroplasty – total or unicompartmental). Total knee arthroplasty is done by replacing the tibial and femoral heads with or without replacing the patella. Unicompartmental knee arthroplasty only replaces the damaged compartment. Approximately 33% of people with knee OA will need knee arthroplasty over their lifetime.

Currently in BC, conventional surgery is used to perform both total knee arthroplasty and unicompartmental knee arthroplasty. However, it has been suggested that robot-assisted knee arthroplasty may improve surgical outcomes (e.g., alignment of components) which, long-term, may result in lower rates of revision surgery (a surgery undertaken if the initial knee arthroplasty fails and some or all of the components utilized in the initial surgery are replaced). Robots are currently utilized in 6 provinces, however the choice to purchase them is driven by local circumstances (e.g., hospital foundation) rather than provincial policy.

The BC Ministry of Health is thus interested in further understanding the effectiveness of robot-assisted arthroplasty. To inform this understanding, C2E2 was commissioned to undertake a clinical evidence synthesis, patient and stakeholder engagement, and economic evidence synthesis and develop a tool to estimate factors associated with cost-neutral adoption.

Clinical evidence:

The clinical evidence synthesis included 6 randomized controlled trials (RCTs) that enrolled 529 patients comparing robot-assisted surgery to conventional surgery. Included studies had a high risk of bias suggesting that the results should be interpreted with caution. Key reported outcomes were revision and alignment – which are less affected by biases -- and patient-reported outcomes such as quality of life and pain (which are more affected by study bias). RCTs reported short-term revision rate (1-5 years) and the results were heterogenous (i.e., studies reported a mix of better, worse and similar revision rates comparing robot-assisted surgery to conventional surgery). With respect to alignment, robot-assisted surgery consistently performed better in both unicompartmental and total knee arthroplasty. With respect to quality of life and pain, no differences were reported between robot-assisted surgery and conventional surgery.

Patient and stakeholder engagement:

No direct patient engagement was undertaken because robot-assisted knee arthroplasty is not currently performed in BC. However, existing reports describing patient experience with robot-assisted surgery (not specific to knee arthroplasty) were reviewed and summarized. Stakeholders who provided input to this HTA included representative of robot manufacturers (n=4), physicians (including surgeons with experience performing robot-assisted knee arthroplasty) and policy makers.

Overall, there is very limited literature published describing the patient experience. Patients reportedly know little about robot-assisted surgery and therefore experience some trepidation, but after the fact report levels of satisfaction similar to conventional surgery.

Both the published reports and stakeholders raised issues around implementation. From an individual perspective, physicians experience a steep learning curve to using robots and desire consistently available technical support from manufacturers. Robot-assisted surgeries require more time per case than conventional surgery. Additionally, it has been suggested that robot-assisted surgery may lead to de-skilling of surgeons (e.g., may forget/be less skilled with a conventional surgery, or moving to a hospital without a robot).

From an organization perspective, the ability to work with robots may be a factor in attracting and retaining top surgical talent. Each robotic system also has a specific physical footprint, and existing operating room space may need to be configured to accommodate a robot, which has capital cost implications. There are potential privacy issues with respect to where the robotic information is processed (within or outside of Canada). Of critical importance however is the "lock-in" effect. When a robot is purchased, there must also be a commitment to purchasing the knee implants themselves from the same manufacturer. Such contractual commitments may affect the entire procurement process in unanticipated ways. Lastly, due to the anticipated surgical volume required to render robot-assisted knee arthroplasty cost-effective, some centralization in service delivery across the healthcare system may be required. If so, this may impact patient travel and equity of access for rural/remote patients.

Economic considerations:

An evidence synthesis of economic studies was undertaken. There is still significant uncertainty around the use of MAKO for total knee arthroplasty. For unicompartmental knee arthroplasty, MAKO and NAVIO ranged from highly cost-effective to potentially cost-effective, with the results affected by surgical volumes (the volume needed to "break even" ranged from 139 (NAVIO) and 320 (MAKO) surgeries per year in the UK, 221-431 surgeries per year with MAKO in the US). [redacted]

The main clinical evidence for the effectiveness of robot-assisted surgery is in the reduction of revision surgery: this is subject to a floor effect. The current Canadian 10-year cumulative revision rate is 4.36% (CIHI data). Observational studies suggest that among patients for whom neutral alignment is achieved they experience a 10-year cumulative revision rate of 2% (i.e., 10-year cumulative revision rate of 2% may be the best achievable revision rate and the margin for improvement is 2.36%). Therefore, robot systems along with the costs of their annual services and implants should be priced considering how much potential for return on investment exists in a specific setting under optimal conditions.

A cost-neutral tool was developed for this HTA. It finds that, given the current prices of robots, services and implants, even if acquiring a robot was cost-free (zero capital investment), concomitant service fees and consumables could only be offset with reductions of 40% to >100% in revisions. Attaining reductions in revision rates of 40% - 100% may be a challenging to achieve.

Chapter 1 Background and Problem

1.1 Purpose of this health technology assessment (HTA) / policy problem

The objective is to evaluate, from the literature, the clinical and cost-effectiveness effectiveness of total or unicompartmental knee replacement performed with the assistance of "robotic technologies" (from any manufacturer of interest for BC) compared with conventional knee replacement, in adults. Also, to investigate qualitatively the implications for surgical training and procurement of both the robots and the knee implants.

Currently, there are no robots in operation assisting knee replacements in BC. [redacted]

1.2 Research questions

1. What is the burden (e.g., revision rates, costs, consequences for the patients and health care system, etc.) of knee replacement?
2. What are the stakeholder (e.g., clinicians, decision-makers, procurement services, etc.) perspectives and experiences with robot-assisted knee replacement (if available), and overall knee replacement management in BC? Questions to consider may include:
    a. What is the current market share of knee implants (and robots, if any) in BC, and how this can be affected by the introduction of robots (e.g. shift, contracts, pricing, etc.)

    b. What implementation, social, cultural, environmental, and/or ethical impacts should be considered with the use of robot-assisted knee replacement?
    c. What are the implications of training surgeons with robots? For example:
        i. Fewer skilled surgeons on conventional replacement?
        ii. What happens if/when the robot fails, and the surgery needs to be performed conventionally if the skill set is not established/maintained?
        iii. What are the considerations for attracting and retaining surgeons?
        iv. What surgical navigation systems can perform both total and/or unicompartmental knee replacement?
    d. What is the market share of the various knee implants utilized in BC across different manufacturers? How might the current market share be impacted by the introduction of robot-assisted replacement (e.g. contractual, pricing, clinical practices, etc.)?
    e. What and where is the existing experience with robot-assisted knee surgery in BC (clinical, procurement, pricing, etc.) if any?
3. What is the current standard of care and conventional surgical pathway, in BC, for patients requiring:
    a. Total knee replacement?
    b. Unicompartmental knee replacement?
4. What are patient perspectives and experiences with robot-assisted knee replacement (if available), and overall knee replacement management in BC?
5. Which provinces and territories are currently publicly providing robot-assisted knee replacement (total and partial)?
6. What is the comparative clinical effectiveness:

a. Robot-assisted total knee replacement vs. conventional total knee replacement?

b. Robot-assisted unicompartmental knee replacement vs. conventional unicompartmental knee replacement?

c. Robot-assisted unicompartmental knee replacement vs. conventional total knee replacement (if existing literature in this context)?

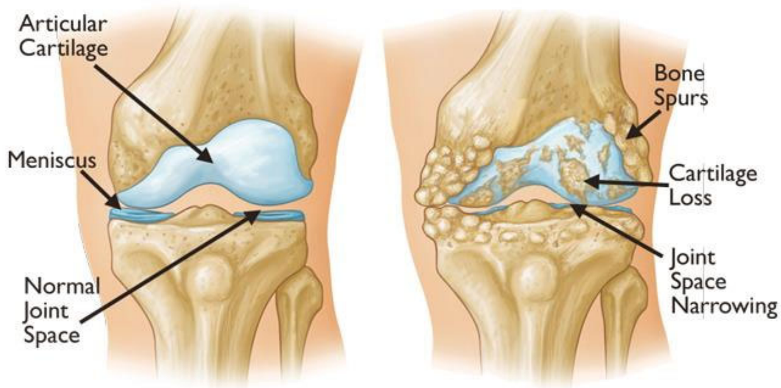
d. What surgical navigation systems can perform both total and/or unicompartmental knee replacement according to the literature?

7. What is the comparative cost-effectiveness of any of the above combinations in the published literature (if any)?

1.3 Natural history of knee osteoarthritis

Osteoarthritis is the most common diagnosis for patients requiring knee replacement. According to the Canadian Joint Replacement Registry (CJRR), 99.3% of knee replacement surgeries were performed due to osteoarthritis in BC.[1] Osteoarthritis is a chronic degenerative disease that affects the joints of the body. Unlike rheumatoid arthritis, osteoarthritis often affects one joint initially.[2] Osteoarthritis is characterized by inflammation caused by the degeneration of tissue and cartilage, as well as bone reshaping that eventually leads to deterioration of joint function (Figure 1-1).[2] The hip and the knee are the joints most frequently affected by osteoarthritis. Symptoms of osteoarthritis include joint pain, stiffness, instability, and motion limitations.

Figure 1-1. Anatomical differences of normal knee and KOA.



Knee osteoarthritis often presents as patients complaining about pain and stiffness in the affected knee. Clinical examination is often used to diagnose knee osteoarthritis but sometimes radiographic images are used to aid in diagnosis.[3] Different organizations have proposed different diagnostic criteria. The National Institute for Health and Care Excellence proposed that "patients can be diagnosed with knee osteoarthritis if they are 45 years or older, have movement-related joint pain and either no morning knee stiffness or stiffness of 30 minutes or less."[4]

The American College of Rheumatology proposed a different set of diagnostic criteria: patients with knee pain, defined as movement-related knee pain, have osteoarthritis if they fulfill one of the following groups of criteria:

1. Crepitus, morning knee stiffness of 30 min or less, and age of 38 years or above
2. Crepitus, morning stiffness of longer than 30 min, and bony enlargement
3. No crepitus, but bony enlargement.

The etiology of knee osteoarthritis is multifactorial. Risk factors include age, sex, weight, physical inactivity, and previous injury.[5]

1.3.1 Condition severity

1.3.1.1 How does the condition affect a patient's quality of life?

An Ontario study analyzed data from the Canadian Community Health Survey and found that people living with osteoarthritis had a lower quality of life when compared with age, sex and rural/urban status-matched cohort in the community.[6] The average reduction of the utility index was 0.16 on a 0-1 scale. Knee pain is an important source of morbidity and cost to the health care system. The same study also found that people living with osteoarthritis had more than double the healthcare-related spending in a calendar year when compared with matched cohort ($2,233 per year vs $1,033 per year).[6]

1.3.1.2 How does the condition affect a patient's expected life?

A population-based study examining the risk of mortality in patients with osteoarthritis found that osteoarthritis increased the risk of mortality (hazard ratio 1.14; 95% CI 1.00 to 1.29).[7] The effect was marginal and the study hypothesized that lack of exercise, depression, anxiety, and poor sleep quality might have contributed to the risk. These were all secondary effects of osteoarthritis. The study was well done but limited by the data which did not provide the severity of the disease.

1.3.1.3 How does the condition affect the caregiver to the patient (quality of life, time resources, etc)?

Knee osteoarthritis can cause disability when it is severe. However, most patients living with knee osteoarthritis are not disabled and live a relatively normal life. In the case of disabling knee osteoarthritis, the condition places a significant burden on caregivers in terms of quality of life and emotional strain.[8]

1.3.2 Condition prevalence

1.3.2.1 How many people live with this condition in BC?

Knee osteoarthritis is a very common condition among people aged 40 or older. It contributes to 80% of cases among all osteoarthritis.[9] A recent study of global disease burden found that the incidence of knee osteoarthritis was 130 per 10,000 person-year in the United States (US).[3] The same study found its prevalence was 15.8% in North America.[3] The prevalence of knee osteoarthritis increased with age with nearly 50% of people 80 or older living with it. It also disproportionally affects the female population. Female incidence and prevalence rates were 1.39 times and 1.69 times higher than the overall average.[3]

Applying the prevalence to the age-specific population of BC estimated by Statistics Canada, there were over 443,000 people in BC, aged 40 and older, living with knee osteoarthritis in 2022. Based on the International Classification of Disease, Ninth Edition (ICD9) code 715, the BC administrative data identified 200,155 patients, aged 40 and older, with some health spending with the condition in the fiscal year 2021-2022.[10]

1.3.2.2 What is the public health impact in BC? Might other populations be affected indirectly either positively or negatively? What population(s) are these?

The condition does not usually affect other members of the public in terms of public safety or personal health risk.

1.3.2.3 Does the condition prevalence match the target population for the intervention?

Despite the estimated prevalence of 200,155 to 443,000 patients living with osteoarthritis in BC (described above), not all patients would need a knee replacement in their lifetime. Approximately 30% of patients with knee osteoarthritis would require knee replacement at some point in their life[11, 12], making up approximately 60,046 to 132,900 patients in BC. Over 75,000 knee replacement surgeries are performed in Canada every year, making it one of the most common surgeries.[13] [redacted] These numbers are limited by the constraints of the BC health system's surgical capacity.

1.3.2.4 Disease burden on the disadvantaged or underserved population

According to stakeholders, people who work in manual labour tend to be affected by osteoarthritis more than average. People with lower income (i.e., those with a lack of disposable income) may experience a more negative impact of osteoarthritis due to a lack of access to non-publicly funded medical services (e.g., physiotherapy) and exercise facilities. A population-based study indicated that the Indigenous population had a higher prevalence of osteoarthritis than the non-Indigenous population.[14] According to the BC Surgical Patient Registry[15], [redacted] (see Appendix A), [redacted]

1.4 Treatment options

The treatment goals for knee osteoarthritis are relief of symptoms, preserving joint function, and improving daily activities and quality of life.[16] The available treatment options include conservative, pharmacological, and surgical treatments. Most patients do not require surgical intervention. A United Kingdom (UK) study in 2012 found that the lifetime proportion of knee osteoarthritis patients receiving a Total Knee Replacement (TKR) was 7.7% and 10.6%

for men and women, respectively.[17] The proportion of TKR has increased over the past decade. A 2019 Spanish study found that the proportion of knee osteoarthritis patients receiving TKR was 30%.[11] A 2021 US study found that the risk of needing TKR was 33%.[12] It was inversely associated with access to physiotherapy. The region in the US where patients had more access to physiotherapy had a lower rate of TKR.[12]

The decision for surgery is a clinical decision. In general, patients are eligible for surgical assessment when pain, stiffness, and disability have seriously affected their daily life; and adequate symptom relief is not achievable with medications and other non-surgical treatments.[18] Potential harm from long term use of pain medication, such as stomach ulcers, risk of cardiovascular disease, and risk of tolerance to opioids, should also be considered. Patients may be considered for unicompartmental knee replacement (UKR) when[19]:

- Degenerative arthritis of the knee affecting one compartment
- >60 years of age
- Body weight <82 kg (180 lb.)
- Low-demand for activities
- Range of motion ≥90°, flexion contracture ≤5°, angular deformity <15°
- Absence of symptoms and signs of inflammatory arthritis

Due to recent technological advances, the criteria have been expanded to younger age, higher weight, and higher levels of activities.[19]

There is no consistent standard of practice across BC. The care pathways vary from region to region, or even within regions. According to stakeholders, family physicians are the primary care providers for patients with knee osteoarthritis in BC. The type of treatment patients receive is largely dependent on accessibility and affordability. For these reasons, it is difficult to estimate the typical treatment pathway that an average patient would experience. In an ideal circumstance, patients should have tried all other non-surgical options before being referred to surgery. However, surgeons have stated that patients were commonly referred for surgery before trying non-surgical options.

An average patient receiving knee replacement surgery due to osteoarthritis in Canada according to CJRR, was between the ages 65 to 75, and 57% of patients are female.[1]

1.4.1 Conventional replacement [aka arthroplasty] (comparator/status quo)

1.4.1.1 Description

The knee is divided into three compartments, medial, lateral and patella. Any one of the compartments or multiple compartments can become arthritic.[20] Instead of replacing all the compartments, UKR replaces only the damaged compartment of the knee.[20]

Figure 1-2. Unicompartmental knee replacement vs. total knee replacement.

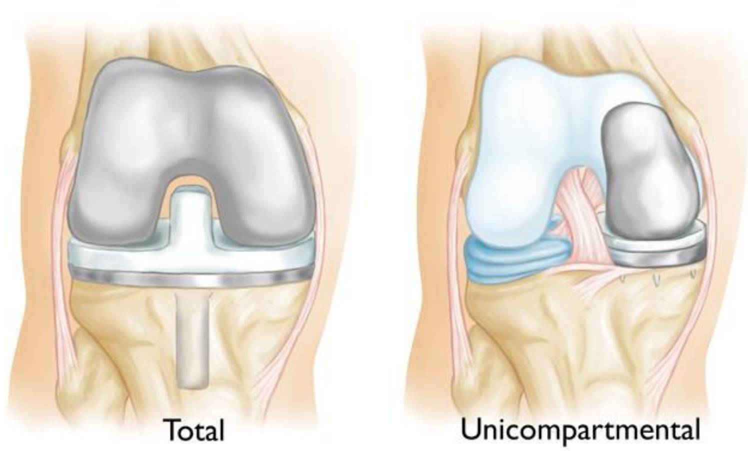


Photo credit: https://orthoinfo.aaos.org/en/treatment/unicompartmental-knee-replacement/

TKR is the more commonly performed surgery consisting of more than 90% of all knee replacements performed in Canada between 2020-2021.[1] TKR is done by replacing the entire tibial and femoral heads of the knee joint with mechanical components. This requires cutting and reshaping the tibial and femoral bone to fit into the replacement parts. TKR can be done without replacing the patella. UKR only replaces the compartment damaged by the disease. As a result, UKR can preserve more of the natural bone, tissue, and ligaments as compared with TKR.[20, 21] The benefits of UKR include less blood loss (20 ml vs 110 ml) and shorter hospital stay.[21, 22] However, UKR is associate with a higher risk of revision when compared with TKR.[21]

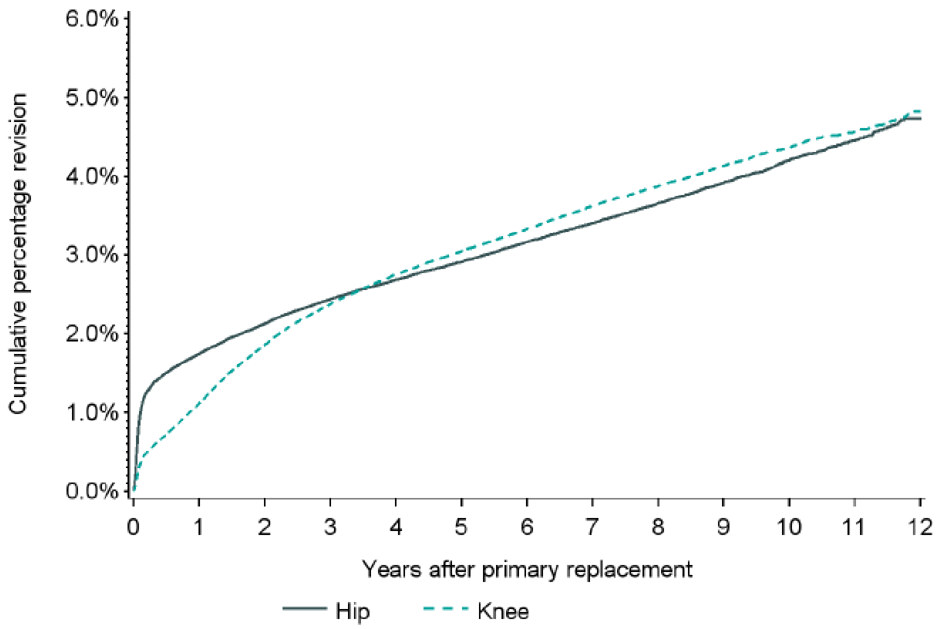
Both UKR and TKR can use cemented or cementless implants. A cemented implant utilizes cement to bond the implant with the bone; a cementless implant utilizes a special rough surface that encourages new bone growth to integrate with the implant. Both types of implants have their pros and cons. A recent study from the National Joint Registry in the UK reported that cementless TKR had higher implant failure when compared with cemented TKR, but the inverse relationship was reported in UKR as cemented UKR had a higher risk of implant failure.[23]

In the case of implant failure, UKR implants can be revised into primary TKR; but TKR can only be revised with a revision TKR. The most common sequence of implants in case of implant failure is primary UKR to primary TKR, and from a TKR to a revised TKR.

The Canadian Institute for Health Information (CIHI) published annual reports on hip and knee replacement surgery[1] based on data from the CJRR. Most implants lasted for the lifetime of the patients. In Canada, the cumulative percentage revision for primary knee replacement is

4.82% after 12 years of the primary replacement (Figure 1-3). The most common reasons for revision are infection, aseptic loosening, and instability.[1]

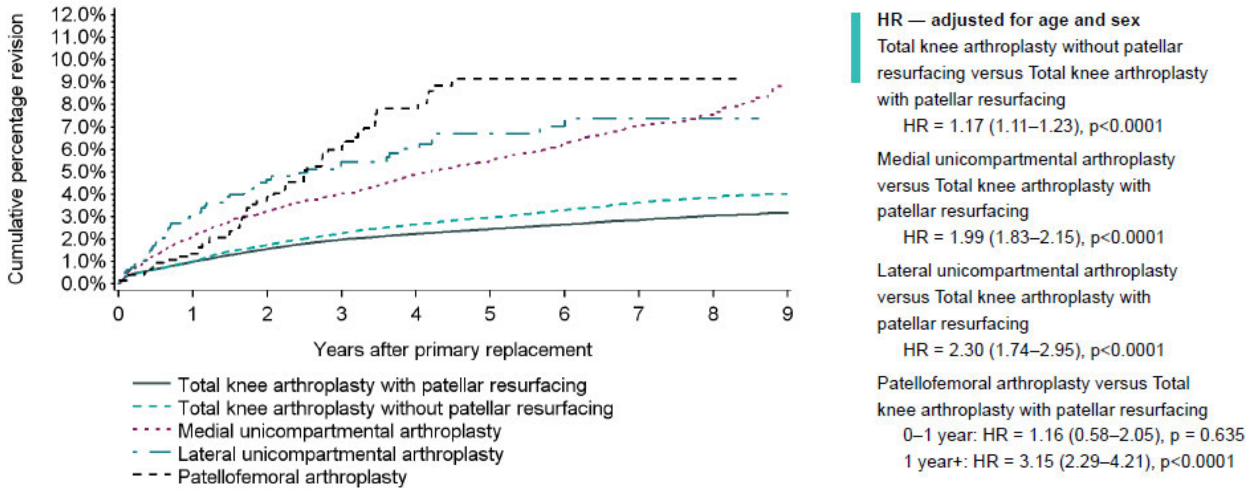
Figure 1-3 Cumulative percentage revision for primary hip and knee replacement due to osteoarthritis, Canada, 2009–2010 to 2020–2021



Sources: Discharge Abstract Database, Hospital Morbidity Database and National Ambulatory Care Reporting System, 2009–2010 to 2020–2021, Canadian Institute for Health Information. Hip and Knee Replacements in Canada: CJRR Annual Report, 2020–2021[1]; Fig 5, page 43.
CJRR = Canadian Joint Replacement Registry

UKR had a higher overall risk of revision in 12 years when compared with TKR, demonstrating the higher technical challenges to “get it right” when partial replacements are compared with total replacements (Figure 1-4).

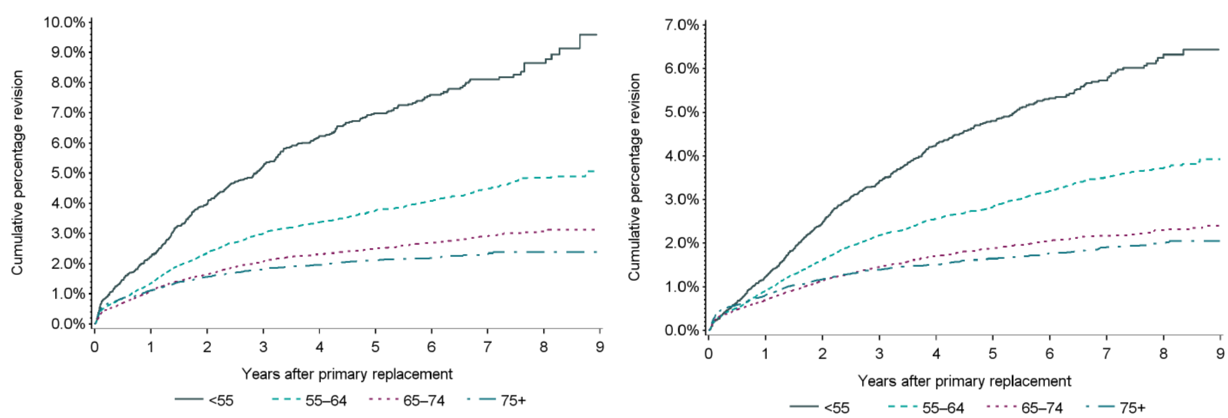
Figure 1-4 Cumulative percentage revision for primary total and unicompartmental knee replacement, by type of procedure (primary diagnosis of osteoarthritis), 2012–2013 to 2020–2021



Sources: Canadian Joint Replacement Registry (Ontario, Manitoba and British Columbia only), Discharge Abstract Database and National Ambulatory Care Reporting System, 2012–2013 to 2020–2021, Canadian Institute for Health Information. Hip and Knee Replacements in Canada: CJRR Annual Report, 2020–2021[1]; Fig 13, page 59.
HR= Hazard ratio; p = P-value; CJRR = Canadian Joint Replacement Registry

Males have a higher revision risk than female patients; and the younger the patient, the higher the revision risk (Figure 1-5).

Figure 1-5 Cumulative percentage revision for primary total knee replacement for male patients (on the left) and for female patients (on the right), by age (primary diagnosis of osteoarthritis)



Source: Canadian Joint Replacement Registry (Ontario, Manitoba and British Columbia only), Discharge Abstract Database and National Ambulatory Care Reporting System, 2012–2013 to 2020–2021, Canadian Institute for

to suppliers or volumes of their products may have unintended consequences on hospital operations.

In BC, when looking either at the 2022 Surgical Registry data[24] (Figure 1-7) and the 2022 Spending data[25] (Figure 1-8) from the Provincial Health Services Authority (PHSA), [redacted]

However, when looking at the hospital-level data (Appendix D), [redacted] any changes in implants required because of the robot choice (i.e. not compatible with the current implant supplier) operationally affects those sites more significantly than others.

Table 1-2 Average prices of knee implants in BC across manufacturers (per surgery)

Manufacturer	Total Knee Replacement		Unicompartmental knee Replacement	
	5-year average	Average in 2022	5-year average	Average in 2022
[redacted]				

Source: Orthopedics Supply Chain – Provincial Health Services Authority (PHSA)[25]
* Disclaimer: average prices were calculated based on total spending by vendor divided by the no. of femoral components purchased from the same vendor in the same period. The results should be interpreted with caution.

All the above are important considerations when deciding the choice and placement of robots across BC hospitals. It certainly impacts the amortized costs of robots per surgery performed, increasingly becoming marketing tools in the implant market.

1.4.2 Robot-assisted knee replacement

Based on the aforementioned BC landscape of knee implants, five robots are potentially of interest for the BC context: ROSA (by Zimmer Biomet), MAKO (by Stryker), SKYWALKER (by Microport), CORI (by Smith & Nephew) and VELYS (by Depuy J&J).

Despite advances in implants, recovery programs, thromboembolic-antibiotic prophylaxis, and computer navigation, studies have shown that up to 20% of patients remain dissatisfied following knee replacement.[26] Accurate implant positioning, balanced flexion-extension gaps, proper ligament tensioning, and preservation of the periarticular soft tissue envelope are important surgeon-controlled variables that affect functional outcomes, implant stability, and long-term implant survivorship.[27]

Conceptually, technology that enables these technical objectives to be delivered with greater accuracy and reproducibility hypothetically may help to further improve outcomes following knee replacement.[27] Advocates of robot-assisted replacement believe that the added cost will be offset in the short term by improved operating room efficiency, decrease pain and expedite recovery, shorter length of stay, and reduced complications.[28] It seems plausible that these technologies could be an effective and cost-effective means of reducing revision risk in clinical populations that are at an elevated risk of revision because of patient-specific demographics (such as younger age at index surgery, elevated BMI, and being a man).[29]

Surgeons may also be hesitant to adopt this technology due to the associated learning curve, slightly increased surgical time, fear of pin site complications, and the initial set-up costs. Irrespective of the form, the use of computer-assisted replacement (i.e. navigation or robot systems) is on the rise worldwide and seems to be here to stay.[30]

However, at present, several reasons make it very difficult to contrast and compare the different robots and extrapolate their results across the category: most of the literature is rather old, these technologies may have changed over time and the robots that generated the evidence may no longer be available in the current market; studies usually evaluate one specific system in one specific setting; robots differ significantly from one another technically and, usually, can only be used for their own brand of implants (and sometimes only with certain models from the same manufacturer). There is currently no legislation, regulation or consensus across manufacturers or surgeons to determine which technologies are simply navigation systems and which ones can be called a robot.

In general, it seems that robots can be classified according to 3 main features: (1) the degree of autonomy (active vs. semi-active vs. passive); (2) the data/image source for the surgical plan (image-based: CT vs. X-ray, imageless); (3) and their mechanisms of cutting control. All of them require some sort of built-in navigation system to determine the surgical plan (e.g. implant size and position) and subsequently guide the bone preparation and activate the cutting control mechanisms.

Fully active robot systems work autonomously to perform the planned femoral and tibial bone resections (e.g. ROBODOC manufactured by THINK Surgical, not available in Canada). The surgeon oversees the bone resection and may activate an emergency deactivation switch if required. *None of the robots of interest for the BC knee implant market is a fully active system.*

Semi-active robot systems enable the surgeon to maintain overall control over bone resection and implant positioning but provide live intraoperative feedback to limit deviation from the preoperative surgical plan. *All of the robots of interest for the BC knee implant market are semi-active systems.*

Robot-assisted knee replacement uses computerized systems at five distinct stages for the accurate execution of the patient-specific surgical plan:[27]

1. With image-based systems, preoperative plain radiographs or CT scans of the knee joint are used to create a virtual three-dimensional reconstruction of the patient's native knee anatomy. With imageless systems, this is performed intraoperatively by the use of the robot navigation system, based on the placement of magnetic spheres in some anatomical landmarks within the surgical field.
2. The surgeon (or for some robots, their product specialist personnel) uses this patient-specific virtual model to plan optimal implant positioning, alignment, and sizing to achieve the desired bone coverage, component position, and limb alignment. Computer software uses this virtual data to calculate femoral and tibial bone resection windows for accomplishing this surgical plan with a high level of precision.
3. Intraoperative bone registration and verification of bony landmarks are used to confirm the patient's osseous knee anatomy before bone resection. In CT-free robot systems, registration is performed by mapping the patient's osseous anatomy onto a generic virtual model of the knee joint, and planning of implant positioning and bone resection is performed intraoperatively. In CT-based robot

knee systems, a patient-specific model of the knee joint is created and osseous anatomy is mapped intraoperatively to confirm bone geometry.

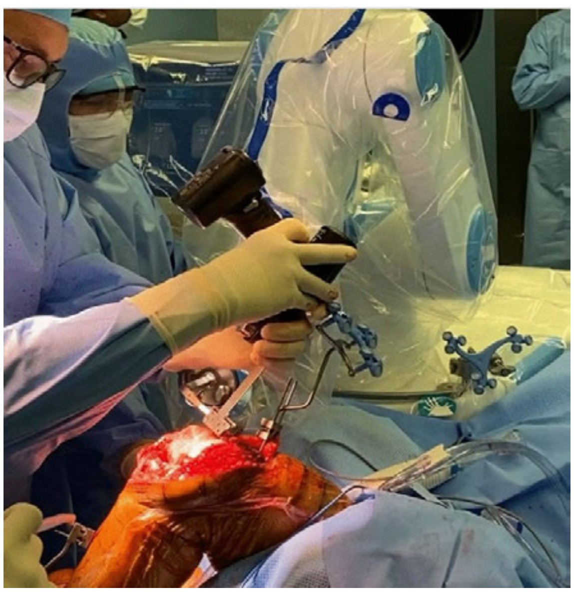
4. Fourth, the surgeon uses the robot system to perform bone resections within the pre-planned boundaries of the femoral and tibial bone windows.
5. Fifth, optical motion capture technology is used to re-assess intraoperative flexion and extension gaps, joint stability, range of movement, and limb alignment. The surgeon can perform live-on-table modifications to bone resection, adjust implant positioning, and fine-tune soft tissue releases to achieve the desired bone coverage, component positioning, knee kinematics, and limb alignment.

1.4.2.1.1 To what degree does the intervention minimize invasiveness

According to comments from Alberta's Evidence Decision Support Program (EDSP), robotic-assisted surgery has some prospect of reducing the invasiveness of knee OA. Some orthopedic robots replace open surgery with a more minimally invasive procedures, while other systems allow the use of a minor for a major open procedure; for instance, robots can enable surgeons "to perform the minimally invasive PKR procedure on some patients instead of TKA".[31]

More details of each prospective robot system follow and are summarized in Table 1-3.

1.4.2.2 ROSA (manufactured by Zimmer Biomet)

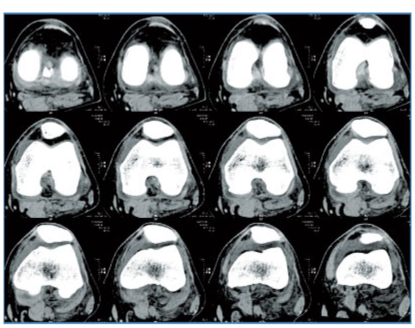


Source: Google images

ROSA is an image-based 2 cart-robot (robotic arm and camera stand) that uses a preoperative 2D X-Ray (or MRI) to create a virtual 3D reconstruction of the patient-specific bone model. The 2D X-ray is not a conventional one and requires a special positioning protocol

[redacted]

1.4.2.3 MAKO (manufactured by Stryker)

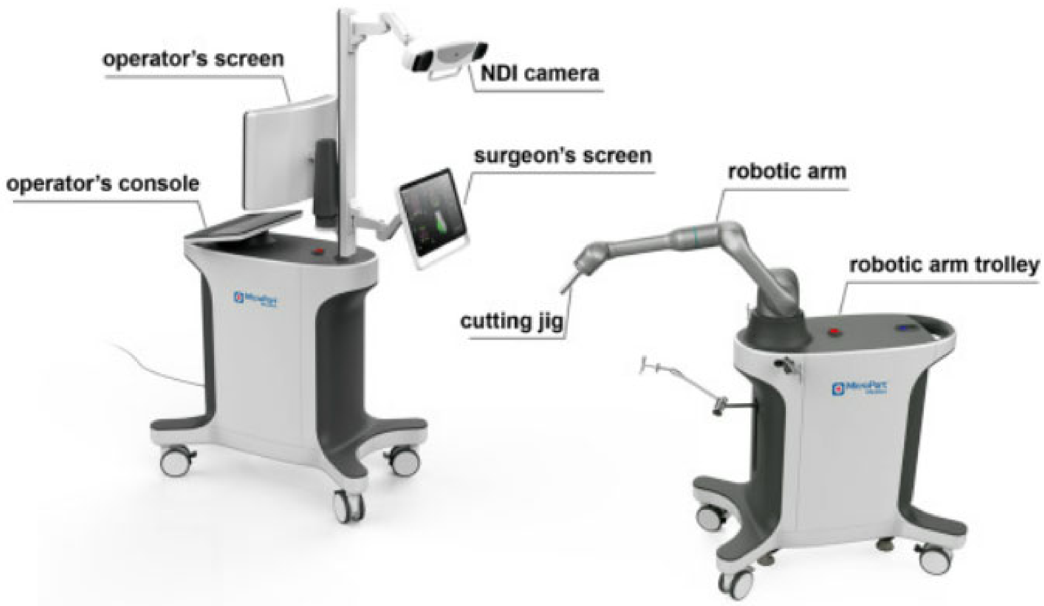


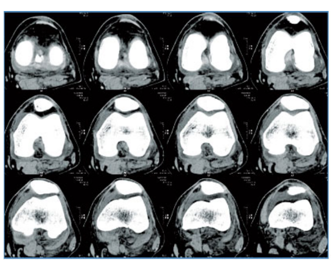
Source: Google images

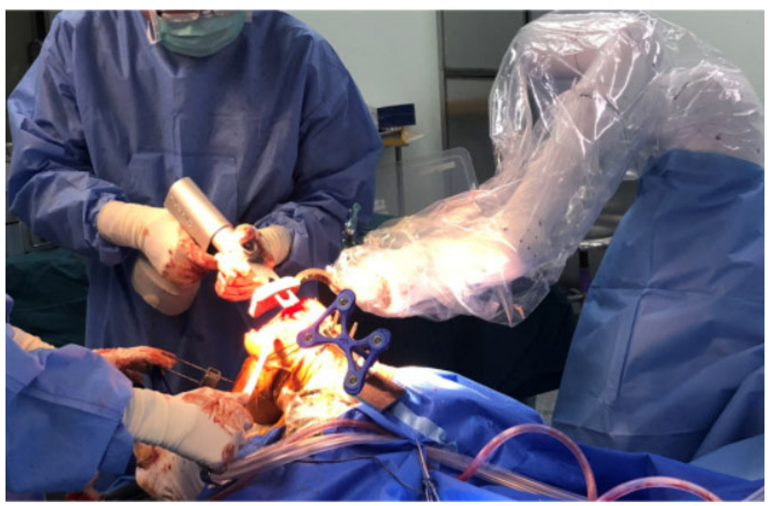
[redacted]

[redacted]

1.4.2.4 SKYWALKER (manufactured by Microport (former Wright Medical)







Source: Google images

Currently, this system is not yet approved by Health Canada and the manufacturer expects the approval to be released in mid-2023. The subsequent information was found online[v].

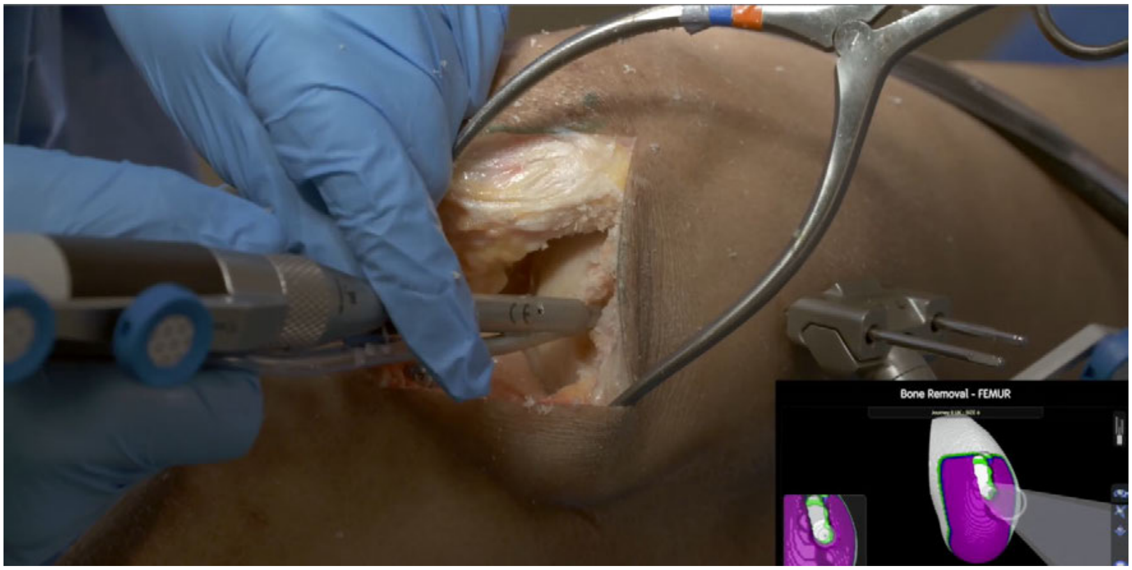
SKYWALKER seems to be an image-based 2 cart-robot (robotic arm and camera stand) that uses a preoperative CT-scan (similar to MAKO) to create a virtual 3D reconstruction of the patient-specific bone model. The robotic arm seems to hold and robotically positioned the cutting guides/jigs to help guide the surgeon's cutting tool (similar to ROSA).

No further information is available at this time.

1.4.2.5 CORI (2nd generation, previously called NAVIO, manufactured by Smith & Nephew(S&N))

NAVIO (1st robot generation – left) CORI (2nd robot generation - right)

v https://www.fiercebiotech.com/medtech/rise-skywalker-fda-clears-surgical-robot-system-orthopedic-procedures

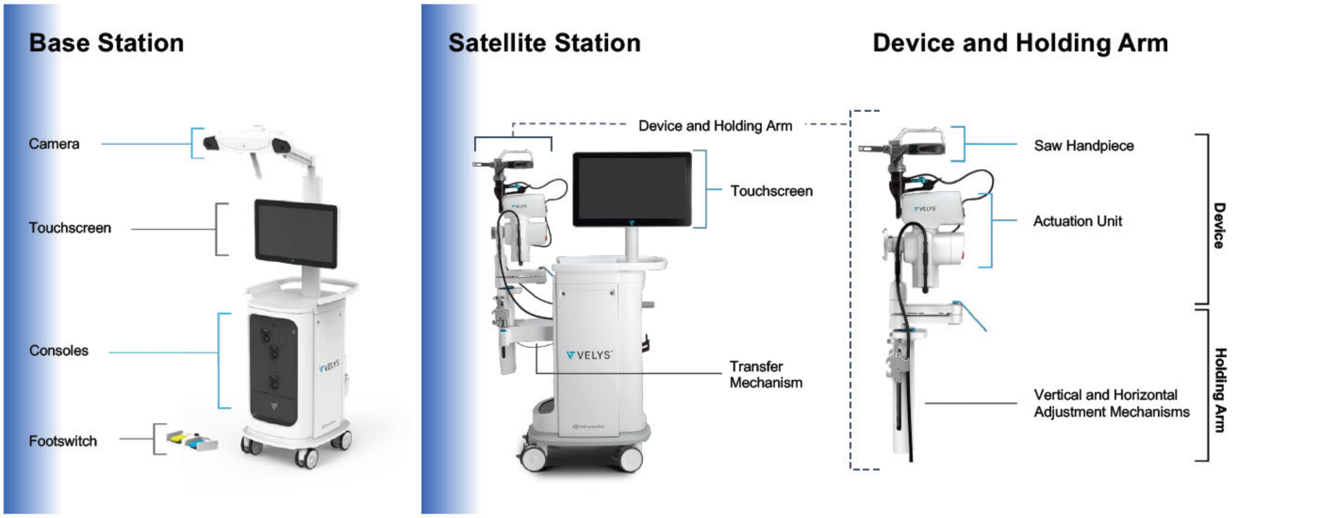


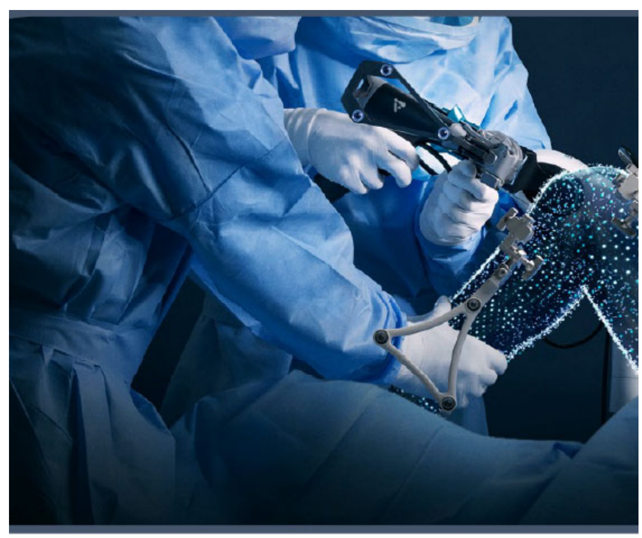
Source: Google images

[redacted]

[redacted]

1.4.2.6 VELYs (manufactured by Depuy / Johnson & Johnson)





Source: Google images

[redacted]

[redacted]

[redacted]

1.5 Emerging technologies that may impact a review of this technology

This question was not addressed in this HTA.

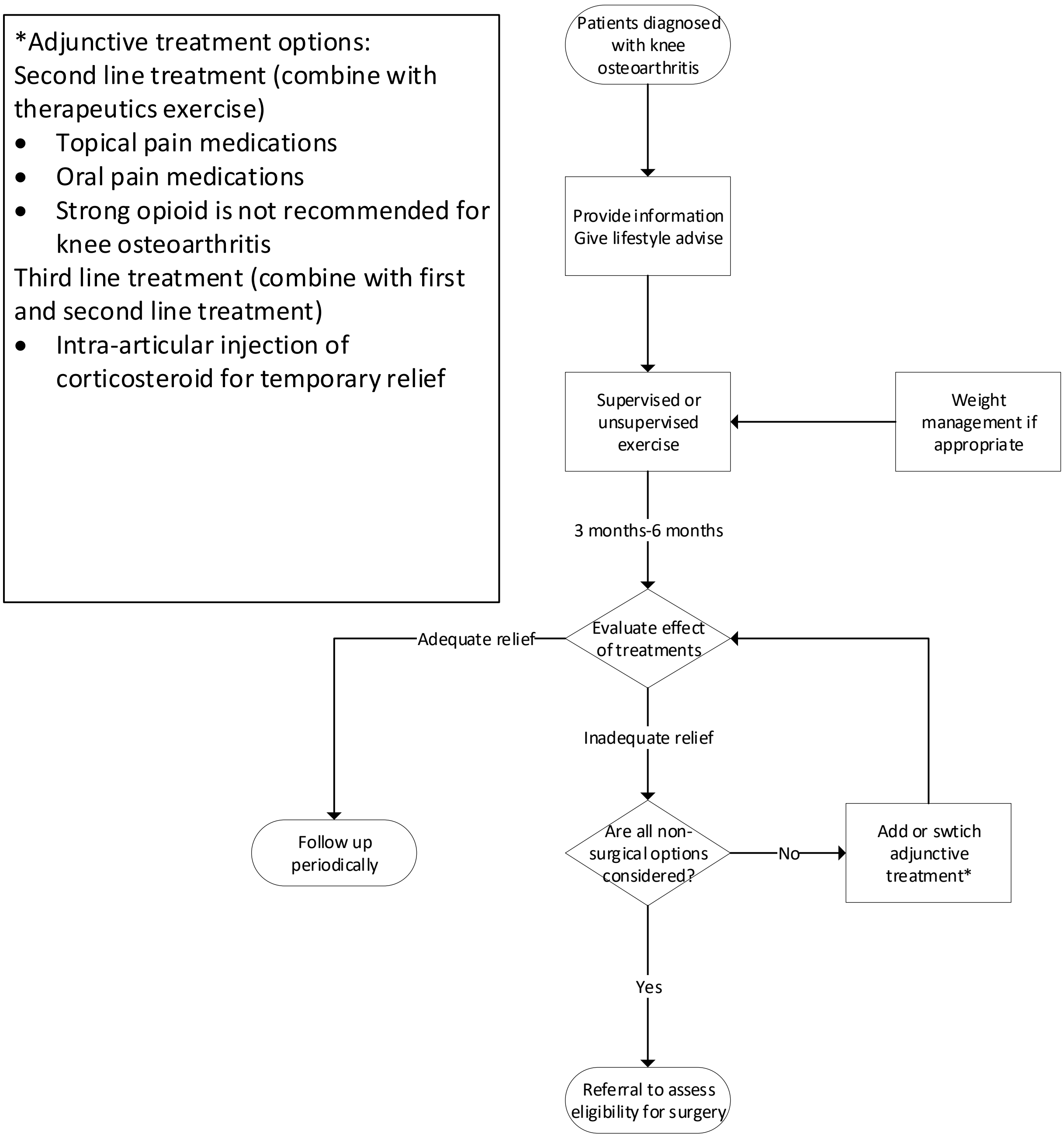
Chapter 2 Jurisdictional Scan

2.1 Care Pathway

The consensus care pathway for BC can be found in Figure 2-1. The treatment goal of osteoarthritis of the knee is to relieve symptoms and improve function. Exercise serves as the first-line treatment of osteoarthritis of the knee and the foundation of the care pathway. When first-line treatment is not adequate to provide relief for symptoms or improve functions, adjunctive therapy can be added. Adjunctive therapies include topical pain medicine, oral pain medicine, and intra-articular injection. When all non-surgical treatment options have been considered, patients who still have significant symptoms and reduced quality of life can be referred to orthopedic surgeons for assessments. The eligibility for surgery is assessed individually. There are no restrictions with respect to age or weight to be considered for joint replacement.[32] The main determinants for eligibility include anatomical abnormality of the knee, previous treatment options, level of pain, and degree of disability.

In a previous project examining the role of a physical activity program for the treatment of knee osteoarthritis, surgeons were interviewed about the care pathway. The surgeons commented that while the described care pathway was the ‘ideal standard’, in reality, there was no single standardized practice in the community. A patient journey might include a discussion with the GP, some self-management for pain, possible referral to private physiotherapy, negotiation with the GP for a referral to a surgeon, and possible surgery that might not have been preceded by a formal exercise program. In summary, the clinicians described the current care standard as a “black box” that no single care provider was responsible for overseeing. As a result, surgeons indicated that it was not uncommon for patients to be referred to surgery as the first option.

Figure 2-1. KOA care pathway.



2.2 Guidelines for the treatment of knee osteoarthritis

No Canadian guideline for the surgical management of KOA was identified. The NICE database was also searched but no guideline was identified regarding the use of robot-assisted joint replacement.

The American Academy of Orthopedic surgeons (AAOS) published a guideline for the surgical management of knee osteoarthritis.[33] The guideline did not find evidence that supports the use of robot-assist TKA or UKA. But the guideline made a note that robot-assist joint surgery might have the potential benefit of reducing pain and improving revision rates in the future.

2.3 HTA jurisdictional scan

2.3.1 Methods

HTA reports from 2012 to 2023 were searched on relevant databases in Canada [e.g., Canadian Agency for Drugs and Technologies in Health (CADTH) (national), Health Quality Ontario (HQO) (Ontario), Institute of Health Economics (IHE) (Alberta), Institut national d'excellence en santé et en services sociaux (INESSS) (Quebec)] and internationally [e.g., the International Network of Agencies for Health Technology (INAHTA), the UK's National Institute for Health and Care Excellence (NICE), Scotland, and Australia]. The following keywords were used: "knee arthroplasty", "knee osteoarthritis" or "robot". No restriction on intervention since there are multiple interventions included in this project. In total, one HTA reports were identified from the CADTH databases.

2.3.2 Results

CADTH published an HTA report in 2022 which included a clinical and economic review of robotic-assisted surgical systems for knee arthroplasty.[34] The report included 10 systematic reviews, three RCTs, and five economic evaluations. The CADTH report concluded that there was no evidence to indicate that robotic-assisted knee arthroplasty provided any additional long-term clinical benefits when compared with conventional surgery. The economic evaluations suggested that robotic-assist knee arthroplasty was cost-effective when clinical inputs assumed improved quality of life and reduced rate of revision when compared with conventional surgery. These clinical inputs were based on assumptions without the support of clinical evidence. Therefore, the CADTH report questioned the accuracy of the economic evaluation.

2.4 Provincial and Territorial jurisdictional scan

2.4.1 Methods

A provincial and territorial jurisdictional scan was performed by reaching out to contacts through the intergovernmental relations secretariat of the BC Ministry of Health. This is supplemented by information obtained through other sources, as described in the sections following.

2.4.1 Results

2.4.2 Implementation considerations: Infrastructure: What approaches to implementation have other jurisdictions used, if applicable?

[redacted]

[redacted]

Using the Intergovernmental Relations secretariat, we conducted a provincial/territorial jurisdictional scan to inquire about policy-level approaches to robot acquisition. Specifically, we asked three questions:

1. Is there an overall policy guiding the adoption of such devices into your publicly-funded healthcare system (e.g., restriction to certain settings); and if so, what are the key details?
2. Is there a target or fixed number of such devices which will be publicly supported?
3. Is there a preference for one type of robot-assisted system over others, and if so for what reasons?

[redacted]

[redacted]

2.4.3 Conclusion

2.4.4 Have other jurisdictions implemented this technology?

[redacted]

Chapter 3 BC context and other stakeholder perspectives

3.1 Objective

To understand the expectations of key stakeholders in BC about the possibility of introducing robot-assisted knee replacement to the province.

3.2 Methods

Data in this section are drawn from interviews with representatives of robot manufacturers/retailers and meetings with physician stakeholders. All meetings and interviews took place in Fall 2022 or Winter 2023; recordings were not taken, but team members kept detailed notes which were reviewed to determine where they spoke to specific assessment questions identified by sub-headings in the sections which follow. We also draw upon qualitative studies of provider perspectives captured by a 2020 CADTH review[34] on the topic of robot-assisted knee surgery, in general.

3.3 Findings

3.3.1 Description of stakeholders

Stakeholders included representatives of 4 manufacturing companies with licensed robots by Health Canada [redacted] and several physicians and policy-makers through the Value of Analysis Team (VAT) and RFP committees from PHSA.

3.3.2 Population, cultural and socioeconomic impacts:

Population, cultural and socio-economic impacts – including impacts on patients' families and community; potentially disproportionate impacts of disadvantaged groups; access for potentially underserved populations; and other forms of inequity -- are addressed in Chapter 4.

3.3.3 Patient experience and autonomy:

3.3.3.1 Does the intervention improve how a patient is treated (respect, dignity, choice of treatment) vs. the comparator?

Addressed in chapter 4.

3.3.4 Environmental considerations:

3.3.4.1 Environmental impact: Carbon footprint: Would in-person follow-up visits and therefore travel be reduced?

Addressed in chapter 4.

3.3.4.2 Environmental impact: Waste: What waste might be generated, and can it be disposed of safely? Does the intervention use reusable consumables or single-use?

3.3.4.3

The robot itself is the major additional product required for the intervention. Robots have been quite recently introduced for arthroplasty, and we came across no information related to the environmental impacts of their manufacturing, or their lifespan (though robotic technology evolves quickly). Presumably, obsolete technologies can be recycled in the same way as other electronic or mechanic products. All systems require more software upgrades than hardware upgrades.

[redacted] disposables are one of the major expenses of knee replacement. All robot-assisted replacements require some additional disposable compared to conventional replacement items which differ across robot systems (e.g. drapes, pins, trackers, plastic spheres, suction systems, etc.). A recent UK study[35] finds that out of the five most common surgical procedures performed by the National Health Service (NHS), knee replacement had the greatest carbon footprint of all, by a considerable margin. Whether or not robot-assisted surgery uses a greater or lesser number of disposables in total than conventional knee replacement surgery was not within the scope of this study.

On the other hand, it was consistently argued that some robot systems would be able to reduce the number of instruments and implant trays needed to be reprocessed/sterilized than with conventional replacement [redacted]). This can have a significant impact on logistical costs [redacted] and human resources workload in the OR and MDRDs. Based on our interview data these costs were taken into account and more details are displayed in Table 1-3 and Table 1-4.

3.3.5 Implementation considerations and operational challenges:

3.3.5.1 Status quo: How is the technology currently provided? How is it funded? What human resources are currently required for the procedure (e.g., admin staff, nurses, etc.)? What are the infrastructure requirements for the procedure (e.g., equipment, OR time, etc)? What are the current challenges? What is currently working well? What MSP fee codes are currently being used?

Robots to assist in knee replacement are not currently in use in BC. [redacted] choosing one particular robot, hospitals will limit their use of implants to those from the same manufacturer; robot systems are not compatible with implants from different manufacturers. This can shift the market share of implants for knee and hip implants within a hospital if the choice of the robot is different from the current supplier of implants, which in turn can have unintended consequences for the procurement of implants and other products. More details about the specifications and business models of the different robots are displayed in Table 1-3 and Table 1-4.

[redacted]

3.3.5.2 Human resources: How would the capacity of service providers be impacted (i.e., Is the relevant expertise available or will clinicians require training)? What human resource recruitment and training would be required?

Human resources workload in the operating room (OR) and MDRDs (Medical Device Reprocessing Department) can be significantly impacted if the robot truly reduces the number of trays needing to be reprocessed.

There have been some concerns expressed around deskilling for surgeons trained to operate exclusively with a robot. The cost-effectiveness of robots seems to be directly correlated to high volumes of surgery (to amortize costs) which likely means they will be placed in high-volume centres. However, some argue that surgeons may lose their skills when required to perform conventional surgery again (e.g. should they move to hospitals without the robot due to the low volume of surgeries in more remote areas). If this occurs it may lead to increased disparity of outcomes between patients seeing between these different sites.

The following points, from the provider perspective, are reported by CADTH in their studies of robot-assisted surgery (note that these studies do not come from the osteoarthritis field):

- Using robots to assist in surgery increases job demands and required technical knowledge; this leads to increased responsibility for some surgical team members such as RNs. Where the nursing workforce is already highly burdened and recruitment is difficult, this might pose a human resources challenge. For the surgeon-operator, robotic assistance reduces tactile aspects of surgery in favour of visual ones; it may require more experienced and confident physicians able to act in the absence of the tactile cues. More ergonomic for the physician
- Robot-assisted surgery requires more time: for set-up, for the surgery itself, and in transitions between surgeries
- There is a significant learning curve; providers need education and training, as well as exposure to a great enough regular volume of procedures to build skills; they also require on-demand technical support → [redacted]

3.3.5.3 Stakeholders: Are there risks (e.g. interest in or against the intervention by stakeholders, vested/financial interests of stakeholders, etc.) associated with key stakeholders (clinicians, nurses, admin, patients, caregivers, etc.) for the adoption or disinvestment of this intervention into routine care?

Robot system manufacturers clearly have an interest in convincing providers to adopt their products. This marketing speaks to some providers, who view robot-assisted surgery with excitement and enthusiasm, and see it as a mark of prestige for their institutions, a demonstration of innovation, and an opportunity to learn new techniques [34].

The generation of electronic data as part of the process may pose certain privacy risks depending upon the individual system selected. With MAKO, for instance – the specific data transfer requirement requires extensive discussion with the IT departments to ensure compliance with laws around patient privacy, data transfer and storage as it includes patient name, date of birth, medical record number (patient identifier) and the CT scan images going outside Canada.

3.3.5.4 Financial: Are there any downstream utilization costs to consider? If so, what is the potential impact? If there is a shift from the private sector to the public sector (or vice versa) as a result of the public provision of this intervention, would this result in negative externalities (e.g. shutting down specialized clinics resulting in lost or shifted jobs...)?

There will be a 'lock-in' effect; providers are only going to choose one system and it may be quite costly or difficult to transition to a different system at a later point in time. The nature of any financial impacts will depend upon the evolution of different technology platforms over time and the shift in market share of implants if the robot of choice is incompatible with the current supplier. There may be also unintended consequences to contracts of other products sold by the manufacturer "losing" market share (e.g. hip implants, other implants and consumables; this may perhaps extend to products required in other forms of surgery or other procedures as well).

3.3.5.5 Infrastructure: What are the infrastructure requirements for the potential implementation scenario(s) (e.g., specific settings (clinics, churches, minimally invasive procedure rooms, etc) or special equipment)?

Acquiring the robot system itself is the main piece of infrastructure required for this intervention. Certain OR configurations are needed to deploy robot systems and their acquisition may also necessarily entail some degree of physical space renovation on the part of the purchaser, but we do not have information at this time to know if, or to what extent, this might be expected with the adoption of robot-assisted knee replacement in BC. The footprint of the different robot system sizes is displayed in Table 1-3

3.3.5.6 Other: What monitoring is in place? What, if any, changes would be necessary to ensure monitoring for this intervention?

Some robot systems do not have any RCTs published. [redacted]

More importantly, currently, there is no MSP fee to distinguish a knee replacement performed with or without a robot. If the expected benefit of the robots in revision is realized, this can introduce a confounder to the data currently collected by the BC Surgical Registry and reported to the Canadian Joint Replacement Registry. It is important to establish a mechanism for tracking the data for robotic-assisted surgery to further evaluate its performance compared to conventional surgery and across the different robot systems.

3.3.6 Ethical considerations

Ethical considerations are outside of the scope of this HTA and were not explicitly researched. Patient privacy issues are noted above (section 3.3.5.3). Some possible population impacts (such as reduction in services to rural areas (see section 4.4.1.1) or deskilling among physicians operating outside metropolitan areas (see section 3.3.5.2) do raise ethical concerns. Whether or not robotic-assisted surgery differs enough from conventional surgery that a separate and distinct consent process should be used is a potential practical ethics issues; it was however not raised in any of the sources of information – Guidelines, patient experience literature, stakeholder interviews – used in this HTA. Given such gaps, these and other emergent issues should be considered with an ethics lens in overall provincial policy decisions related to the potential introduction of robotic-assisted knee arthroplasty.

Chapter 4 Patient Experience

4.1 Objective

To gain an understanding of the outcomes related to robot-assisted knee replacement which are important to patients, to guide the evaluation of the clinical literature and health policy. As robot-assisted knee surgery is not currently available in BC, we did not conduct direct patient engagement for this report. Instead, we are summarizing the literature on patient experiences and perspectives as reported in work conducted by CADTH in 2020-2023.

4.2 CADTH rapid review of patients' experience

4.2.1 Methods

In 2020, CADTH conducted a qualitative synthesis of literature[36] on the general research question of "How have people undergoing surgery with the use of robot systems, and the surgical teams using them, experienced engaging with these systems?" [p3] The literature search was conducted in three databases – Medline, PsychInfo and Scopus – limited to English language articles published from January 2010 to January 2020. It was supplemented by a targeted literature search focused on gynecological and urological procedures, which resulted in a reference list (2022[37]).

In light of this previous work, we commissioned an updated search, English-language only, of articles published between January 1, 2020 and March 23, 2023[38]. The research question was, "What literature is available that explores the perspectives, expectations, and experiences of people in need of knee replacement regarding accessing and engaging with robot-assisted knee replacement?" Three databases were searched: MEDLINE, Scopus, and CINAHL.

4.2.2 Overall results from CADTH rapid review (summary)

Here we summarize the findings from CADTH's 2020 qualitative synthesis,[36] supplemented with insights derived from papers identified by the 2022 gynecology-urology reference list [37] and the 2023 knee replacement reference list, [38] which were retrieved and reviewed by our team.

Fourteen (14) studies with qualitative designs met the inclusion criteria; all from the peer-reviewed search, none from grey literature. "Five of the included studies were from the UK, four were from the USA, one from Turkey, one from Australia, one from South Korea, one from Norway, and one study reported occurring across Europe" (2020; p. 6). There were no Canadian studies, but CADTH suggests that the consistency of themes emerging from the synthesis allows transferability with at least some confidence (2020; p. 11).

Among studies, 11 were on the perspectives of surgical teams, with only two on patient perspectives (in both cases men treated with prostate surgery, in Australia and the UK). One study of 25 people was conducted with participants drawn from the UK general population. The overall quality of the studies was rated as good, though 2 were rated by CADTH as of clearly poor quality (including 1 of the 2 patient studies).

Only 3 studies indicated which robot was assisting (all being Da Vinci), and only 6 of 14 studies specified which type of surgery was being undertaken. These were all in the area of urology, prostate or colorectal; CADTH notes that gynecology and urology are the main fields in which robots are being used (2020; p.3).

The updated reference list found no additional qualitative studies, published from 2020-2023, which directly addressed knee replacement patients' experiences with a robot-assisted surgery. The search did identify 6 articles which were potentially of relevance but which did not meet the inclusion criteria. Three of these reported the experiences of nurses only, and one reported on surgeons performing abdominal rectopexy. Two publications[38, 39], derived from a UK study on barriers and facilitators to the implementation of robot-assisted surgery, provided some confirmation and extension of the findings observed by CADTH in 2020, and are described in more detail below. These publications report the views of 35 NHS surgeons, healthcare providers and policy-makers; one of the two publications also included a focus group with surgical trainees and a focus group with 8 members of the British public.

On the patient side, CADTH's primary conclusion is that "due to limited published literature exploring their experiences, the patient perspective was an overall gap in this review" – "there is a clear gap in qualitative evidence on the patient experience of RS [robotic-assisted surgery]" (2020; p.11). Another review similarly found a "dearth of studies" from the patient perspective (Moloney et al, 2020[41]). Moloney et al's review concludes that, in terms of patient satisfaction, there were no clear differences overall between conventional and robot-assisted surgeries, and where there were differences reported it was unclear if these were due to the modality itself (robot vs other) or to patient experiences of the surgical outcomes.

The two patient studies suggested that the male participants who opted for robot surgery did so because it was minimally invasive and they believed it would be more effective for their preferred treatment outcomes, though they felt that they needed more information to truly understand the choices. Wu et al (2022)[42] also found in a study of robot-assisted procedures in China that patients tended to have an "insufficient understanding of the surgical methods". Two studies with female patients (drawn from the gynecology literature) both concluded in strikingly similar language that these patients generally had confidence and trust in robot-assisted surgery and recovered quickly – it was "a piece of cake" (Herling et al[42], 2016; Kurt et al, 2021[44]). Nonetheless, Kurt et al reported some "ambivalent feelings" or trepidation, due to the newness of the techniques and patients' lack of knowledge about them. In particular, there were concerns about whether or not the surgeon would be absent from the operating theatre itself – i.e., if the robot were to be operated remotely (concerns also echoed in the study by Lawrie et al, 2022a[38] as well as Wu et al[42]).

The above studies were gender-specific, though seemingly comparable in findings. The one general population study reviewed by CADTH explicitly contrasted male and female perspectives on robot-assisted surgery, which tentatively pointed to possible gender differences, with females being less trusting and more concerned about safety.[44] As well, "while female participants viewed RS [robot-assisted surgery] as de-humanizing, males humanized surgical robots and exhibited a sense of anthropomorphism in relation with RS" (CADTH, 2020; p. 11). Since public participants had no direct experience with robot surgery, their knowledge was derived primarily from the media.

Providers in the Lawrie et al study (2022a[38]) also perceived that the public was relatively uninformed about the nature of robot-assisted surgery – that it saw robots "in a disproportionately positive manner" and education was needed. Views directly from members of the public remain quite scantly reported but confirmed CADTH's earlier finding (2020) that, to the extent that the general public is aware of robot-assisted surgery, their limited knowledge derives primarily from media depictions.

4.3 BC-specific patient experience

As robot-assisted knee replacement is not currently conducted in BC, we concluded that it would be unlikely to easily identify patients who would be able to speak to their experience and share perspectives. Our patient partner took part in our deliberations about this.

4.4 Conclusions

4.4.1.1 Population, cultural and socioeconomic impacts:

The two papers by Lawrie et al [38, 39] both touch briefly on questions of health inequities and access. They report that providers hold mixed views on the centralization of robot-assisted surgery. Many see this as important to generate the volume of procedures needed for providers to develop proficiency, and may be partly affected by the need for ORs to be of a certain size and design to comfortably accommodate the robot carts; others fear that it may decrease access to poorer and remote areas. This is an ethical issue (Esperto et al, 2021[45]). There was some confidence however, that “long-term implementation could reduce overall health inequalities by widening access to minimally invasive surgery and enabling operations to be conducted on more patients, with positive outcomes” (2022b[39]). It was also perceived by some respondents, correctly or otherwise, that robot-assisted surgery promised better outcomes for frail, elderly and obese patients (2022b[39]) — this would contribute to greater equity for certain disadvantaged groups.

4.4.1.1.1 To what degree does the intervention improve a patient's family/community?

Given that there is minimal difference in treatment outcomes between robot-assisted surgery and the comparator, it is unlikely that the intervention impacts the family or community more than conventional replacement.

4.4.1.1.2 To what degree does the intervention improve/reduce access or outcomes for underserved populations?

Addressed in 4.4.1.1 above.

4.4.1.1.3 Does this technology alleviate or exacerbate inequities that already exist for different patient populations accessing care?

Addressed in 4.4.1.1 above. Should the introduction of robot-assisted knee replacement be accompanied by centralization of service delivery, this may increase the burden on patients from rural or remote areas to access care.

4.4.1.2 Patient experience and autonomy:

4.4.1.2.1 To what degree does the intervention reduce patients' feelings of being unsafe, uncomfortable or uneasy?

As noted, given the relative newness of robot-assisted procedures, some studies find a degree of patient trepidation on finding that this will be their treatment. On the other hand, the qualitative evidence available indicates that patients find the treatment itself to be easy and that they have faith in the quality of work and prospects for recovery.

4.4.1.2.2 The treatment improves the patient's ability to live independently and on their own terms?

Given that outcomes between conventional and robot-assisted knee replacement are largely similar, no improvements in patients' ability to live independently should be expected due to the intervention.

4.4.1.2.3 Does the intervention improve how a patient is treated (respect, dignity, choice of treatment) vs. the comparator?

No evidence on this point was identified.

4.4.1.2.4 The extent to which the intervention impacts the patient experience and autonomy outside of the specific health benefits; this may also include caregivers and immediate social group

There is no evidence identified from the patient's perspective which speaks to this point or suggests differences between robotic-assisted or conventional surgery.

4.4.1.2.5 To what degree does the intervention reduce pain (physically, emotionally and/or psychologically)?

No evidence to suggest a difference between treatment and intervention.

4.4.1.2.6 Does the technology impact patient safety (positively or negatively)?

According to CADTH, some of the issues which have arisen during surgery include "malfunction of the setup joint, robot arm, camera and power errors, monocular monitor loss, metal fatigue and malfunction of surgeon's console handpiece, and software incompatibility" (CADTH, 2020[36]; p12). It is for these reasons that providers demand, and appear to receive, on-site technical support from robot system manufacturers.

Ultimately, there is no evidence to suggest a difference between robotic-assisted and conventional surgery.

4.4.1.3 Environmental impact:

4.4.1.3.1 Carbon footprint: Would in-person follow-up visits and therefore travel be reduced?

There is no indication in the identified patient experience literature about changes in follow-up visits. Again, should greater use of robot-assisted replacement go along with increased centralization in overall service delivery, it would be expected that more patients would be travelling greater distances to be treated.

4.5 Overall Conclusions about Public and Patient Perspectives and Experience

Very little has been published on patient perspectives; what there is comes mostly from studies in other specialties than orthopedics. As orthopedics deploys robots in a way different than the other types of surgery, the transferability of findings cannot necessarily be assumed.

The general public's knowledge of robotic-assisted surgery is shaped mainly by the media. Those receiving these surgeries want and need information from their providers. It is unclear how well or completely this is being provided and probably there is considerable variability across hospital sites. Patients do report being satisfied with robot-assisted surgery, though there is not enough information to determine if there are any substantive differences from conventional surgery; nor is there enough to assess if there are any differences in experience across any socio-demographic groups. The most common concern reported by patients across studies appears to be whether or not the surgeon will be absent from the operating theatre. None of the robot systems of interest to the BC implant market allow for remote operation of the robot; the surgeon has to be present to operate it.

Chapter 5 Assessment of Evidence

The HTA conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH) was identified from the health technology assessment (HTA) jurisdictional scan (see Chapter 2). The 2022 CADTH HTA[33] included a comprehensive literature review and included 10 SRs, 72 RCTs, and 5 economic evaluations. Overall, the evidence indicates that robot-assisted knee arthroplasty, compared with conventional knee arthroplasty, is associated with decreased length of hospital stay and increased operative time, but not yet improvements in quality of life and reduced rates of surgical revisions. The 2022 CADTH HTA[34], included several studies (10 SRs, 72 RCTs, and 5 economic evaluations) which support the decreased length of hospital stay and increased operative time, but not yet improvements in quality of life and reduced rates of surgical revisions associated with robot-assisted knee arthroplasty. However, it aggregated the results from all robots found in the literature, as well as aggregating total and unicompartmental knee replacement. Early key stakeholder engagement pointed to the fact that most of the robots which generated this evidence are no longer on the market or not available in BC. Each robot seems to only work with the implant from the same manufacturer, therefore, their selection needs to be relevant to the BC implant market. Also, they emphasized the need to look at patient outcomes and think about the policy questions disaggregating total and unicompartmental knee replacements. This is because the technology seems promising to shift the clinical practice towards more unicompartmental knee replacements, to preserve the joint, soft tissues and ligaments, and postpone the need for total knee replacement and revisions, especially when the incidence of knee replacement is increasing in the population in general, but more concerningly, in younger patients over time.[1, 47]

All of the above have unintended consequences for the joint procurement of robots and implants. Therefore, the CADTH report served as the starting point and it was complemented by any studies published subsequently. The overall evidence was separated according to the different surgical techniques and identified the robots relevant to the BC context.

5.1 Objectives

Clinical review: to evaluate the clinical effectiveness of robot-assisted knee replacement when compared with conventional replacement in the management of knee osteoarthritis (defined as those not assisted by any robot system or navigation system).

Economic review: to summarize previously published evidence on the cost-effectiveness of robot-assisted replacement in the management of osteoarthritis of the knee.

5.2 Methods

5.2.1 Inclusion criteria

Table 5-1. PICOS.

	Clinical review	Economic review
Population	Adults aged ≥18 years with knee pain who have failed nonoperative management, requiring knee replacement (total or partial/partial) due to any cause (e.g., osteoarthritis, rheumatoid arthritis, psoriatic arthritis, trauma)	
Intervention	Primary replacement performed using any robot systems from any manufacturer relevant to BC (e.g., Zimmer Biomet's ROSA, Stryker's MAKO)	
Comparator	Conventional surgery performed without any navigation system	
Outcomes	The precision of component placement Soft tissue damage and systemic inflammatory response Blood loss Operative time Postoperative pain and opioid use Postoperative functional status and mobility, range of motion Length of stay Pain Post-operatory emergency room visits and readmissions Complications Revision rates Quality of life Patient satisfaction	Cost-effectiveness outcomes QALY ICER ICUR Resource utilization Time away from work Impact on caregivers

Note: ICER = Incremental cost-effectiveness ratio; ICUR = Incremental cost-utility ratio; QALY = quality-adjusted life years

The available evidence from the 2022 CADTH HTA report[34] and a 2022 CADTH horizon scan [38] were used as a guide for the decision to update the review, as well as a cross-reference. The primary sources of data for this review were RCTs. Potential relevant nonrandomized studies were searched and identified if needed. Lower levels of evidence, such as single-arm studies, were considered hypothesis-generating and determined to be insufficient for policy decision-making.

In the economic review, only studies that conducted a full economic evaluation were included, regardless of which robot it used, to provide an overview of how other jurisdictions have designed economic evaluations on robots for knee replacement; this refers to studies that conducted a comparative analysis of the differences in both costs and benefits across treatment groups.

Non-RCT costing comparison studies will be excluded but referenced in the future, if relevant to the robot systems of interest for BC, to contextualize cost components important for implementation aspects and the design of future economic evaluations.

5.2.2 Exclusion criteria

- Non-English-language publications
- Abstract/conference proceedings
- Letters and commentaries
- Studies without an appropriate comparator arm
- Cost comparisons from non-RCT type studies

5.2.3 Literature search overview

An experienced medical information specialist developed and tested the search strategies through an iterative process in consultation with the review team. Aspects of the strategies from the two recent CADTH reports[34, 48] were reviewed and incorporated where appropriate.

Using the multifile option and deduplication tool available on the OVID platform, we searched Ovid MEDLINE® ALL, Embase, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials on December 21, 2022. All strategies utilized a combination of controlled vocabulary (e.g., “Robotic Surgical Procedures”, “Arthroplasty, Replacement, Knee”, “Knee”) and keywords (e.g., “robot-assisted”, “arthroplasty”, “knee replacement”). Vocabulary and syntax were adjusted across the databases. We limited results to the publication year and/or update period from January 1, 2022. Animal-only records and opinion pieces were removed where possible. Results were downloaded and deduplicated using EndNote version 9.3.3 (Clarivate Analytics) and uploaded to MS Excel.

We performed a separate grey literature search of targeted sites from CADTH Grey Matters[49], Google Scholar, ClinicalTrials.gov and the ICTRP Search Portal on December 29th and 30th.

5.2.4 Study selection

One reviewer screened titles and abstracts and then full texts according to the inclusion and exclusion criteria set in the PICOS question. The study flow was summarized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

One reviewer extracted all the data for clinical outcomes, while a second reviewer extracted all the data from economic analyses. Data were cross-checked for errors by the two reviewers. Any discrepancy was resolved by discussion when needed.

5.2.5 Quality assessment

The risk of bias was assessed using the Cochrane Risk of Bias tool. Five categories of risk were assessed including selection bias, detection bias, performance bias, attrition bias, and reporting bias.[50]

5.2.6 Data synthesis

For the clinical review, when appropriate, dichotomous outcomes were analyzed by using risk ratio (RR) or odds ratio (OR). When we found a statistically significant RR or OR we also calculated the risk difference (RD) and number needed to treat (NNT) for the outcome when possible. Continuous outcomes were analyzed using weighted mean difference (WMD). If meta-analysis was not possible, the clinical data were summarized.

The following data were extracted from economic studies when appropriate: country of origin, study type, model type, reported outcomes, source of funding, currency, time horizon, discount rate, interventions, costs, QALYs, incremental effects, ICERs, ICURs, main assumptions, perspective, and cost and resource utilization and modelling of effectiveness. Data were qualitatively summarized.

5.2.7 Subgroup analysis

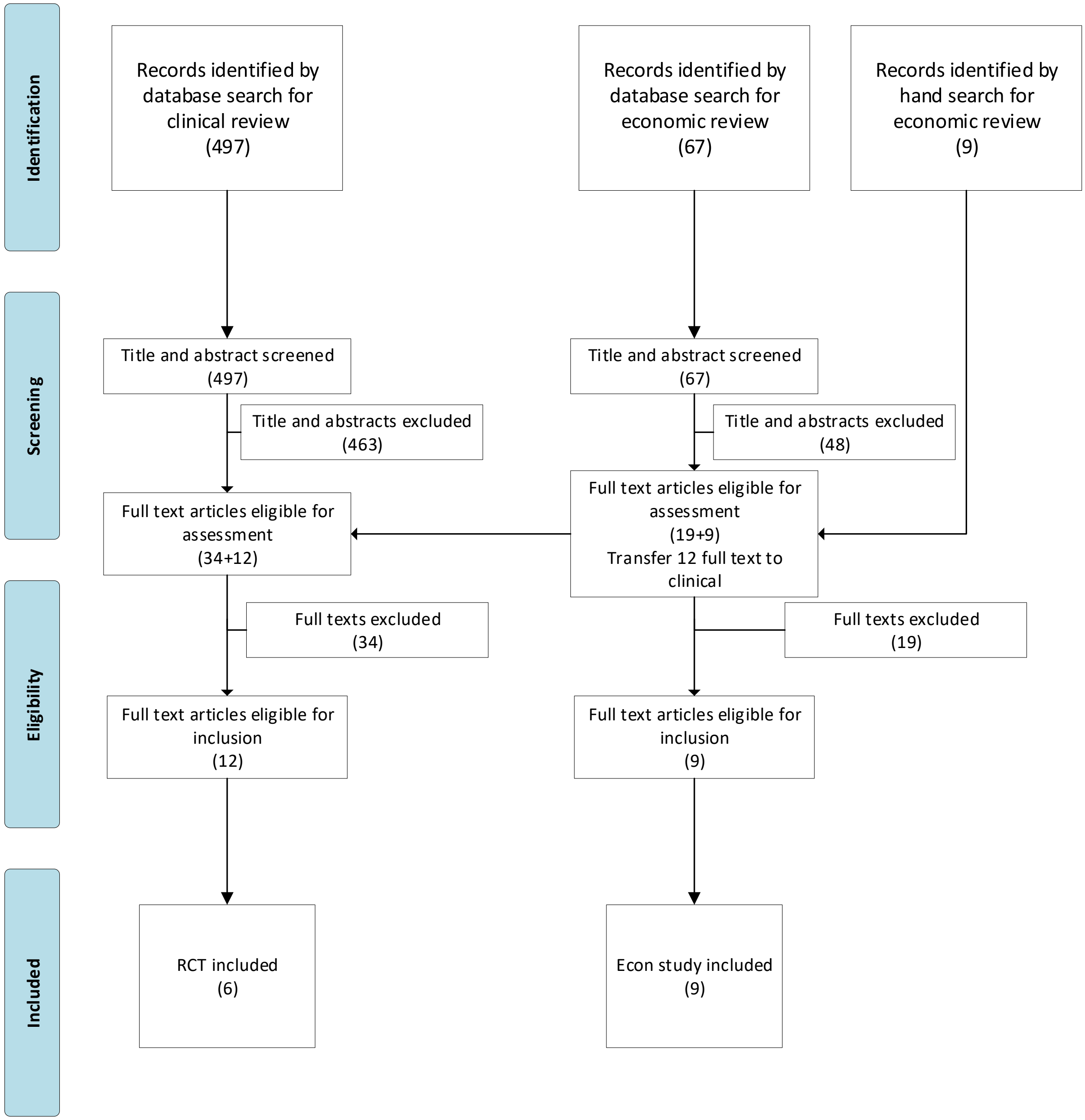
No subgroup analysis was performed.

5.3 Search results

A total of 497 abstracts were screened for clinical review, of which 34 records were retrieved for full-text review. An additional 12 full texts from economic study screening and seven full texts from CADTH were retrieved. Six RCTs published in 12 articles met our inclusion criteria.[50-61]

A total of 67 abstracts of economic abstracts were screened, of which 19 records were retrieved for full-text review. Another 9 articles were manually identified among their references and from the CADTH 2022 HTA[34]. From the 28 articles full-text screened, 9 primary economic evaluations met the inclusion criteria[29, 62-69], most of which were already included in previously published systematic reviews (CADTH HTA 2022[34] and Bai et al 2022[70]).

Figure 5-1. PRISMA diagram



5.4 Clinical effectiveness

5.4.1 Description of included studies

Six RCTs that enrolled 529 patients published in 12 articles were included in this clinical review (the RCTs are referred to as follows: Bell 2016, Banger 2020, Kayani 2021, Batailler 2022, Vaidya 2022, and Thiengwittayaporn 2022).[50-61] All of the included RCTs enrolled adult patients with primary osteoarthritis undergoing knee replacement surgeries. Two RCTs (Bell 2016 and Batailler 2022) included patients undergoing unicompartmental knee replacement (UKR); four RCTs (Banger 2020, Kayani 2021, Vaidya 2022, and Thiengwittayaporn 2022) included patients undergoing Total Knee Replacement (TKR). Banger 2020 compared bi-unicompartmental knee replacement (bi-UKR) with TKR; bi-UKR replaced both medial and lateral compartments separately, but it was essentially a TKR. In general, patients were randomized to robot-assisted or conventional surgery. Three RCTs used MAKO (Bell 2016, Banger 2020, and Kayani 2021); and the other three RCTs (Batailler 2022, Vaidya 2022, and Thiengwittayaporn 2022) used NAVIO.

The baseline demographic reported in the RCTs was brief. In general, patients were in their late 60s with Body Mass Index (BMI) between 27 to 32 kg/m^2. The description of the key characteristics of the RCTs can be found in Table 5-2..

Table 5-2. Baseline demographics

Study name	**Robot type**	**Intervention**	**Comparator**	**Intervention sample size**	**Comparator sample size**	**Age**		**Female %**		**BMI**	
						Int	**Con**	**Int**	**Con**	**Int**	**Con**
Banger 2020/ Blyth 2021/ Banger 2022	MAKO	r-biUKR	cTKR	38	42	68.7	70.5	53%	52%	31.7	32.6
Vaidya 2022	NAVIO	r-TKR	cTKR	32	28	62.2	59.9	75%	86%	27.1	27.9
Bell 2016/Blyth 2017/ Montesharei 2018/Gilmour 2018/Banger 2021	MAKO	r-UKR	cUKR	70	69	62.5	61.7				
Batailler 2022	NAVIO	r-UKR	cUKR	33	33	67.1	65.6	36%	63%	26.4	28.3
Kayani 2021	MAKO	r-TKR	cTKR	15	15	68.7	67.9	53%	47%	27.5	27
Thiengwittayaporn 2022	NAVIO	r-TKR	cTKR	77	77	69.1	69.1	92%	80%	28	27.7

Note: BMI = body mass index; cTKR = conventional total knee replacement; cUKR = conventional unicompartmental knee replacement; r-biUKR = robot-assisted bi-unicompartmental knee replacement; r-UKR = robot-assisted unicompartmental knee replacement; Int = intervention; Con = control.

5.4.2 Critical appraisal

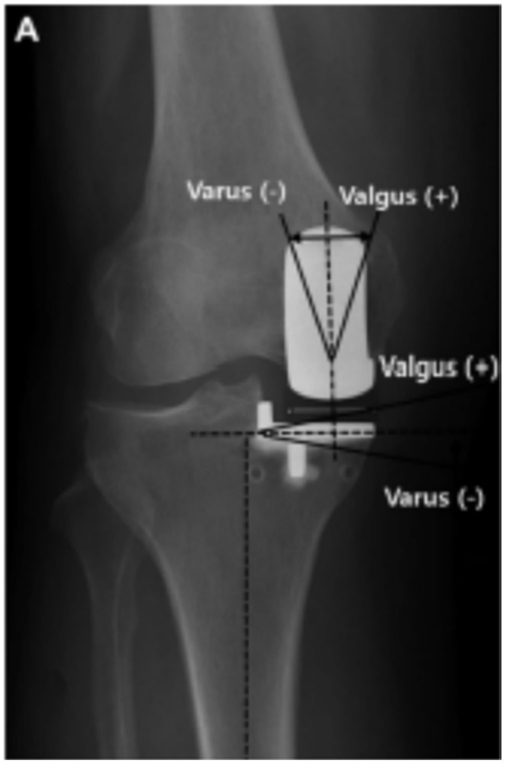
The included RCTs had a high risk of performance and detection bias due to the open-label nature of the RCTs. Performance bias means that investigators and patients are aware of the treatment allocations. Performance bias had the most influence on subjective outcomes such as symptoms scales, and quality of life. Objective outcomes, such as alignment assessment and revision, should not be influenced by performance bias as much. The reporting of the demographics in the RCTs was brief in most RCTs. It was difficult to determine if the randomization was compromised since demographic differences would be a useful tool to determine the integrity of the randomization procedure.

5.4.3 Alignment

Alignment is an important measurement for knee replacement. Malalignment is a risk factor for implant failure and revision.[71] An observational study found that malaligned TKR implants had two to six times the risk of revision in 8 years compared with aligned TKR implants. Another observational study found that malaligned UKR implants had two to five times the risk of revision in 5 years with higher baseline risk.[73]

Alignment is measured using radiography. An outlier is defined as the implant having more than a two or three-degree deviation from the neutral position. Alignment is measured in several positions, for example, the coronal plane and sagittal plane of the femoral and tibial implants are common measurements for alignment. Figure 5-2 is an example of how the femoral implant position is assessed using radiography.[73] In the absence of long-term data for revision, the number of patients with acceptable alignment (2° or 3° of freedom) can be used to predict the risk of revision. It is more technically demanding for the alignment of UKR than TKR. Therefore, historically, UKR has a higher risk of malalignment and revision over time.[1]

Figure 5-2. Radiographic assessment of implant femoral and tibial alignment.



5.4.3.1 TKR

Three RCTs reported the alignment assessment in various types of measurement. This section was separated by types of robot and type of measurement.

5.4.3.1.1 MAKO

Banger 2020[52] reported the proportion of patients within 2° of the neutral position in all measurements of alignment at three months after surgery. This was a very conservative measurement as it only included patients who were within a two-degree deviation from the neutral position among all six measurements (i.e. the coronal, sagittal and axial plane of the femoral component and tibial component). As a result, fewer patients met this criterion for a neutral alignment. Only 47% of patients in the MAKO group and 24% of patients in the conventional surgery group were in neutral alignment after surgery. The MAKO group had significantly more patients within 2^{o} of the neutral position than the conventional group (p=0.045).

5.4.3.1.2 NAVIO

Vaidya 2022 and Thiengwittayaporn 2022 reported on various alignment assessments comparing NAVIO TKR with conventional TKR at three months.[60, 61] In summary, more patients in the NAVIO group were in neutral positions than patients in the conventional group. The proportion of patients in neutral positions in various measurements can be found in Table 5-3..

Table 5-3. The proportion of patients in neutral alignment after TKR with NAVIO vs. conventional TKR

		Vaidya 2022	Thiengwittayaporn 2022
Intervention sample size		32	77
Control sample size		28	77
% of patients who has <3º change from neutral in Hip-Knee-Ankle alignment outcomes	NAVIO	0.969	0.947
	Control	0.714	0.844
	P value	*NR*	*0.035*
% patients <2º of femoral coronal target position	NAVIO		0.787
	Control		0.675
	P value		*0.086*
% patients <2º of femoral sagittal target position	NAVIO		0.973
	Control		0.714
	P value		*<0.001*
% patients <2º of tibial coronal target position	NAVIO		0.84
	Control		0.662
	P value		*0.009*
% patients <2º of tibial sagittal target position	NAVIO		0.853
	Control		0.636
	P value		*0.002*
% patients <3º of femoral coronal target position	NAVIO	1	0.907
	Control	0.813	0.844

	P value	*NR*	*0.179*
% patients <3º of femoral sagittal target position	NAVIO		0.973
	Control		0.753
	P value		*<0.001*
% patients <3º of tibial coronal target position	NAVIO	0.969	0.933
	Control	0.821	0.818
	P value	*NR*	*0.027*
% patients <3º of tibial sagittal target position	NAVIO		0.907
	Control		0.714
	P value		*0.002*

Note: NR = not reported.

5.4.3.2 UKR

One RCT comparing MAKO with conventional UKR reported the proportion of patients within 2º of neutral alignment in various measurements. Table 5-4. and Table 5-5 list the proportion of patients with neutral alignment in various measurements and various degrees of acceptance. A higher proportion of patients in a neutral position indicates a better outcome.

Table 5-4. The proportion of patients within 2° of neutral alignment after UKR MAKO vs. conventional UKR

Study name	Robot type	Intervention	Comparator	% patients within 2 degrees of femoral coronal target position		% patients within 2 degrees of femoral sagittal target position		% patients within 2 degrees of femoral axial target position		% patients within 2 degrees of tibial coronal target position		% patients within 2 degrees of the tibial sagittal target position		% patients within 2 degrees of tibial axial target position	
Follow-up time (months)				3		3		3		3		3		3	
				Int	Con	Int	Con	Int	Con	Int	Con	Int	Con	Int	Con
Bell 2016	MAKO	r-UKR	cUKR	0.70	0.28	0.57	0.26	0.53	0.31	0.58	0.41	0.80	0.22	0.48	0.19
		P value		0.0001		0.0008		0.0163		0.097		0.0001		0.0009	

Note: Con = control; cUKR = conventional unicompartmental knee replacement; Int = intervention; r-UKR = robot-assisted unicompartmental knee replacement.

Table 5-5. The proportion of patients within 4° of neutral alignment after UKR MAKO vs. conventional UKR

Study name	Robot type	Intervention	Comparator	% patients within 4 degrees of femoral coronal target position		% patients within 4 degrees of femoral sagittal target position		% patients within 4 degrees of femoral axial target position		% patients within 4 degrees of the tibial coronal target position		% patients within 4 degrees of the tibial sagittal target position		% patients within 4 degrees of the tibial axial target position	
Follow-up time (months)				3		3		3		3		3		3	
				Int	Con	Int	Con	Int	Con	Int	Con	Int	Con	Int	Con
Bell 2016	MAKO	r-UKR	cUKR	0.97	0.47	0.85	0.50	0.84	0.56	0.93	0.75	0.97	0.50	0.82	0.33
		P value		NR		NR		NR		NR		NR		NR	

Note: Con = control; cUKR = conventional unicompartmental knee replacement; Int = intervention; r-UKR = robot-assisted unicompartmental knee replacement.

5.4.4 All-cause revision or reoperation

Three RCTs reported revision from six months to five years.[52-54] The evidence presented mixed results and is difficult to interpret. Two RCTS reported more revisions in the robot-assisted groups while one RCT reported more revisions in the conventional surgery group:

- Banger 2020 reported 2.6% revision in the robot-assisted arm (MAKO) compared to 2.4% revisions in the control group at 3 months (p=1.0);
- Bell 2016 reported zero revisions in the robot-assisted arm (MAKO) compared to 8.7% revisions in the control group at 5 years (p=0.0001).
- Batailler 2022 reported 12.1% revision in the robot-assisted arm (NAVIO) compared to zero revisions in the control group at 6 months (p=0.12);

Revision is a rare event that takes a decade to accumulate. Short-term data, even five-year data, can be misleading and often presented with conflicting results. The conflicting results may have been caused by small sample sizes and short duration of follow-up. Short-term revision after the surgery could be due to surgical complications or the learning curve of new technology. The data for revision can be found in Table 5-6.

Table 5-6. All cause revision or reoperation

Study name	Robot	Intervention	Comparator	Cumulative revision (n/N)									
Follow-up time (months)				3		6		12		24		60	
				Int	Con	Int	Con	Int	Con	Int	Con	Int	Con
Banger 2020	MAKO	r-biUKR	cTKR	0.026	0.024								
Bell 2016	MAKO	r-UKR	cUKR					0.000	0.000	0.000	0.029	0.000	0.087
Batailler 2022	NAVIO	r-UKR	cUKR			0.121	0.000						

Note: Con = control; cTKR = conventional total knee replacement; cUKR = conventional unicompartmental knee replacement; Int = intervention; r-biUKR = robot-assisted bi-unicompartmental knee replacement; r-UKR = robot-assisted unicompartmental knee replacement.

5.4.5 Patient satisfaction

Two RCTs reported patient satisfaction. Batailler 2022 reported at 6 months; Bell 2016 reported a 5-year percentage of patients who were satisfied with their implants.[53, 54] The percentage of patients who were satisfied with their implant was not different between the robot-assisted group and the conventional group.

- At 6 months, 88% satisfaction was reported in the robot-assisted group; 85% satisfaction was reported in the conventional group (p=0.7).
- At 5 years, patients in the robot-assisted group reported 78% satisfaction in daily living and 69% satisfaction in recreational activities; while the conventional group reported 76% satisfaction in daily living and 65% satisfaction in recreational activities (p>0.05).

5.4.6 Quality-of-life

Only Bell 2015 and Banger 2020 reported quality of life and both used EQ-5D VAS as the measurement tool.[52, 54] Banger 2020 reported quality of life at 3 and 12 months. Bell reported quality of life at 5 years. In summary, quality of life was not different between the robot-assisted group and the conventional group in any of the measurements (p>0.05). The data on quality of life can be found in

Table 5-7..

Table 5-7. Quality of life.

Study name	***Robot type***	***Intervention***	***Comparator***	***Mean EQ-5D VAS (SD)***					
Follow-up time (months)				3		12		60	
				Int	Control	Int	Control	Int	Control
Banger 2020	MAKO	r-biUKR	cTKR	78.0 (21.18)	82.5 (12.56)	74.9 (22.3)	78.9 (15.7)		
Bell 2016	MAKO	r-UKR	cUKR					80.3 (16.4)	76.3 (18.2)

Note: cTKR = conventional total knee replacement; cUKR = conventional unicompartmental knee replacement; Int = intervention; r-biUKR = robot-assisted bi-unicompartmental knee replacement; r-UKR = robot-assisted unicompartmental knee replacement; SD = standard deviation.

5.4.7 Symptom scales

Bell 2016, Banger 2020, and Batailler 2022 reported the results of various symptom scales that included Pain VAS, American Knee Society Score, Oxford Knee Score, Forgotten Joint Score, UCLA Activity Scale, International knee society score, New knees society score.[52-54] The data can be found in the attached Excel file. The symptom scores were not different between the robot and conventional groups in multiple time points except that the robot-assisted group had better scores in the first 3 months. However, this can be the result of a high risk of performance bias. Performance bias is referred to the potential impact of the knowledge of the allocation of treatment. Patients might evaluate the outcomes such as symptom scales differently because of their view toward the intervention they received. In summary, both groups reported similar symptom scores in the long term.

5.4.8 Length of Hospital stay

Bell 2016[54] reported that patients in the MAKO group had 0.54 days (p=0.07) shorter hospital stays than those in the conventional surgery group after TKR. The absolute numbers for the duration of the stay in both groups were not presented in the studies (only the difference).

5.4.9 Operative time

Banger 2020 and Thiengwittayaporn 2022 reported the robot-assisted groups (both MAKO and NAVIO) had longer operating times than the conventional group.[52, 60] Banger 2020 reported that the average time for operation in the MAKO group was 159.4 minutes (SD 20.1) while the average operating time in the conventional group was 96.8 minutes (SD 15.8) ($p<0.001$). Thiengwittayaporn 2022 reported the operating time for NAVIO and the conventional group was 70.1 minutes (SD 12.1) and 61.9 minutes (SD 10) respectively ($p<0.001$).

5.4.10 General practitioner utilization

Bell 2016[55] reported the primary care utilization of patients in the MAKO group and conventional group three months after the operation. The proportion of patients who had accessed primary care in three months after knee replacement was 30% in the MAKO group, and 45% in the conventional group ($p=0.09$).

5.4.11 Safety

Only one RCT reported complications at three and 12 months.[56] The proportion of patients who experienced any complications at three months in the robot-assisted group and the conventional group were 29.4% and 31% respectively; at 12 months, there were 55.9% and 52.4% respectively ($p=0.76$).

5.4.12 Summary of findings

- Six RCTs enrolled 529 patients published in 12 different articles included in this clinical review (all adults with primary knee osteoarthritis undergoing knee replacement surgeries). Two RCTs (Bell 2016 and Batailler 2022) included patients undergoing UKR; four RCTs (Banger 2020, Kayani 2021, Vaidya 2022, and Thiengwittayaporn 2022) included patients undergoing TKR. Three RCTs used MAKO (Bell 2016, Banger 2020, and Kayani 2021) and three RCTs (Batailler 2022, Vaidya 2022, and Thiengwittayaporn 2022) used NAVIO in the robotic-assisted arms.

- The included RCTs had a high risk of performance and detection bias due to the open-label nature of the RCTs. Performance bias means that investigators and patients were aware of the treatment allocations. Performance bias had the most influence on subjective outcomes such as symptoms scales, and quality of life. Objective outcomes, such as alignment assessment and revision, should not be influenced by performance bias as much.
- Overall, the most significant outcome that showed the benefit of robot-assisted knee replacement was alignment. The robot-assisted knee replacement consistently performed better in alignment when compared with conventional surgery in both UKR and TKR.
- The RCTs showed inconsistent results in revision due to the small sample size and short duration.
- The robot-assisted surgery also showed a longer average operative time when compared with conventional surgery.
- For all other outcomes, robot-assisted knee replacement showed comparable results with conventional surgery.

5.4.13 Clinical conclusion

Only two robots of interest for BC have been tested in the RCTs. Since robot-assisted surgery provided comparable results in the short-term outcomes to conventional surgery, the risk of revision becomes one of the most important long-term outcomes to consider. However, the risk of revision requires at least a decade to accumulate enough events to show consistent results, RCTs that lasted only a few years do not allow enough time to assess long-term outcomes (i.e. usually the 10-year risk of revision for each specific robot). In this case, a risk factor for revisions could serve as an alternative in the absence of long-term revision data. The malalignment of implants is a risk factor for revision.[73] Therefore, having better alignment could potentially reduce the risk of revision.[71, 72] Both MAKO and NAVIO provided better alignment of implants when compared with conventional surgery. This suggested that using MAKO and NAVIO could potentially lower the risk of revision in the long term.

Using alignment as a proxy for long-term outcomes warrants caution. Alignment is only one of the factors that influence the risk of revision. The estimates from changing alignment alone might not reflect the whole reality.

5.5 Cost-effectiveness

Nine primary economic evaluations met the inclusion criteria [29, 62-69] and an overview of the characteristics of the included study is provided below and summarized in Appendix I and Appendix J.

5.5.1 Robot-assisted TKR

5.5.1.1 Description of included economic studies

Five cost-utility analyses (i.e. Cost per QALY) published between 2020 and 2023 ***compared robot-assisted TKR with conventional TKR***, from the USA[29, 62-64] or UK payer perspectives[65]. They were all model-based simulations (Microsimulation-Markov or Markov models, Appendix I).

The inputs for the treatment effect of the robots were derived mostly from evidence from ROBODOC and CASPAR robots (the only robots with evidence from RCTs). The only model that also included some evidence from MAKO robot[64], derived the evidence from 2 (non-RCT) comparative observational studies[xi], and aggregated it to the body of evidence from ROBODOC. Lastly, one model[65] was not robot specific and performed a threshold analysis to find the price, or treatment effect, any robot would have to assume/produce, to be considered cost-effective given a certain baseline revision rate. Three models simulated the treatment effect by a direct decrease in revision rates[62, 63, 65]. Two models used the effect of the technology on implant alignment to indirectly affect revision rates [29, 64]. The evidence of alignment on revision rates

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[xi] Marchand RC, Sodhi N, Bhowmik-Stoker M, et al: Does the robotic arm and preoperative CT planning help with 3D intraoperative total knee arthroplasty planning? J Knee Surg 2019;32:742-749; Jeon SW, Kim KI, Song SJ: Robot-assisted total knee arthroplasty does not improve long-term clinical and radiologic outcomes. J Arthroplasty 2019;34:1656-1661.

was derived from observational studies with average follow-up times of s 8 ± 4 years (range, 2–17 years, n=980)[xii] and 6.6 ± 3.5 years (range 2-22.5 years, n= 6,070)[xiii].

The inputs for the costs of the robots were derived from ROBODOC, CASPAR, MAKO or not-robot specific (i.e. threshold analysis to find the price any robot would have to assume/produce to be considered cost-effective given a certain baseline revision rate).

Their time horizons ranged from 10 years to a lifetime and used 1-year cycles. The patient population across these models varied in age (from all ages (microsimulation) to specific cohorts of 60, 65, 70 and 71-year-old patients). One model[29] incorporated site-specific aspects such as the risk profile of its patients for revision (age, BMI and sex), caseload and risk-prioritized policy for the use of robots (i.e. to a % of the cases instead of all cases). The other models started with an assumption around the volume of surgeries per year (ranging from 25/year to 600/year) to define the costs per case of the robots; or explored how different caseload thresholds for the use of robot-assisted surgeries can affect the site-specific cost-effectiveness. They all included upfront costs for the capital acquisition of the robot, except for the UK model[65] which estimated a threshold for incremental costs of robots (per case) to be considered cost-effective.

5.5.1.2 Results for r-TKR vs. cTKR

The results as reported in the primary studies comparing robot-assisted TKR to conventional TKR are summarized in Table 5-8.

[xii] Lee BS, Cho HI, Bin S il, Kim JM, Jo BK. Femoral component varus malposition is associated with tibial aseptic loosening after TKA. Clin Orthop Relat Res. 2018;476:400-407.
[xiii] Fang DM, Ritter MA, Davis KE. Coronal alignment in total knee arthroplasty: just how important is it?. J Arthroplasty 2009;24:39–43. doi: https://doi.org/10.1016/j.arth.2009.04.034.

Cost-effectiveness estimates varied widely depending on the willingness-to-pay (WTP) thresholds assumed for adoption, surgical volumes and the risk levels of the patients.

At a WTP threshold of $50,000/QALY in the USA perspective (and time horizon ranging from 10 years to lifetime), some of the primary studies[62-64] found robot-assisted TKR to be cost-effective in sites with volumes of 42 to 70 surgeries per year, with a considerable amount of uncertainty in probabilistic analysis (likely to be cost-effective from 2.18% to 67.5% of the time). Hickey et al 2023[29] incorporated patient risk factors for revision (age, BMI, sex) in a risk-prioritized treatment protocol in which the technology would be used for a certain proportion of patients per site (instead of all patients); also taking into account each site-specific surgical volumes. Their results showed that for lower-risk populations, for robots to be cost-effective (at a WTP = $63,000/QALY) surgical volume would need to be of at least 600 TKRs per year, and only used for 27% to 32% of the cases (i.e. 162 to 190 TKRs per year). Robot-assisted TKR was not estimated to be cost-effective below this range (per-procedure capital costs are too high) because they are amortized over a volume of surgeries that is too low, and above this range (per-procedure variable costs are too high) because the variable costs are incurred in each robot-assisted surgery (e.g., disposables) and therefore surpassing the savings. For higher-risk populations, for robots to be cost-effective (at a WTP = $63,000/QALY) surgical volume would need to be of at least 100 TKRs per year, and only used for 20% of the cases (i.e. 20 TKRs per year). And from a marginal cost-effectiveness ratios (MCER) analysis, robots would be cost-effective if used up on 94% of these patients; or marginally cost-saving if used on up to 40% of these patients.

A threshold analysis from the UK perspective[65] found that at a WTP threshold of £20,000-£21,000/QALY, if the robot costs are equivalent to ₤10,000/patient, the robot would need to lower their current revision rates by 50% or improve quality of life after (unrevised) primary TKR by 5% on average.

Table 5-8 Summary of results from the identified economic studies (per person) – robot-assisted TKR vs. conventional TKR

SR	-	-	CADTH 2022[34]	CADTH 2022[34]	CADTH 2022[34]
Study	**Hickey et al 2023[29]**	**Hua et al 2022[63]**	**Rajan et al 2022[64]**	**Vermue et al 2021[64]**	**Burn et al 2020[65]**
Robot	ROBODOC+CASPAR (For Costs and Effects)	MAKO (Costs)/ ROBODOC (effects)	UNCLEAR (Costs) / ROBODOC+ MAKO (effects)	MAKO (Cost) / ROBODOC +CASPAR (Effects)	Not specific to a single ROBOT (threshold analysis)
Time Horizon	20 years	10 years	Lifetime	20 years	Lifetime
Currency	2021 US$	2021 US$	2020 US$	2020(?) US$	2020(?) £
ICER/QALY	NR (graph format with ranges)	$41,331	Low volume (13/y): $256,055 Mid volume (100/y): $15,658 High volume (200/y): $2,331	Mid volume (70/y): $376,145 High volume (253/y): <$50,000	NR
Value (as a function of WTP and a number of other variables) *High value = cost-effective*	WTP = $63,000/QALY **For lower risk populations (age at index in years 76±7; BMI in kg/m² 23±3; 94% women)** - High-value ICER (includes capital costs) only in practice sizes of at least 600 patients per year; utilization between 27% to 32% of patients - Not estimated to be cost-effective below this range (per-procedure capital costs are too high), and above this range (per-procedure variable costs are too high).	WTP = $50,000/QALY Cost-effective when case volume exceeded 49 cases per year; probabilistic sensitivity analysis suggested robot-assisted TKR had a 50.04% chance of	WTP = $50,000/QALY - The robot-assisted revision rate would have to increase from the base case of 0.6% to 1.6% for conventional TKR to become the preferred procedure. - Cost-effective when institutional case volume >42 per year - Probabilistic Analysis - cost-effective 67.5% of the time." WTP = $100,000/QALY	WTP = $50,000/QALY Cost-effective 2.18% of the time (assuming 70 TKRs per year)	WTP = £/QALY At current lifetime costs of health care for conventional TKR (£6,060), current lifetime patient utility (10.3), current lifetime revision rates in the NHS

given a certain WTP	- MCER (does not include capital costs)** - marginally cost-effective if used on up to 90% of patients **For elevated risk populations (age at index in years 65±9; BMI in kg/m2 32±6; 54% women)** - High-value ICER for practice sizes as small as 100 patients per year; utilization of at least 20% of patients - MCER - marginally cost-effective if used on up to 94% of patients, and marginally cost-saving to use it on up to 40% of patients**	being the more cost-effective procedure INMB: $129	- The robot-assisted revision rate would have to increase from the base case of 0.6% to 2.2% for conventional TKR to become the preferred procedure. - Cost-effective when institutional case volume >24 cases per year. - Probabilistic analysis cost-effective 68.5% of the time.	system (5.8%), and NHS willing to pay up to an additional £10,000/patient for the robot, to achieve cost-effectiveness the robot would need to: -Improve post-primary unrevised QoL by 5% on average, or -Decrease the revision rates by 50%.

(?) Currency year not stated, assumed the year of the article submission; SR = systematic review; QALYs=Quality-adjusted life years; ICER=incremental cost-effectiveness ratio; MCER=marginal cost-effectiveness ratio (in this study does not include capital costs); WTP=willigness-to-pay; NR=not reported; TKR = total knee replacement; r-TKR = robot-assisted total knee replacement; INMB = incremental net monetary benefit; ** MCER from the Hickey et al 2023 study can be interpreted for BC as a proxy for settings in which the robot is offered in consignment funding models and no capital costs incurred

5.5.2 Robot-assisted UKR

5.5.2.1 Description of included economic studies

Three cost-utility analyses (i.e. cost per QALY) and one cost-effectiveness analysis (i.e. cost per revision avoided) published between 2016 and 2022 ***compared robot-assisted UKR with conventional UKR****; and one of the cost-utility analyses also* ***compared robot-assisted UKR with conventional TKR.*** They are all model-based simulations (Markov models) from the USA or UK perspectives (Appendix J).

The inputs for the treatment effect of the robots were derived from non-RCT evidence. For NAVIO, both models used evidence from the same retrospective multicenter cohort study [xiv]; for MAKO the model derived evidence from a prospective multicenter cohort study [xv]; and the last model derived the evidence from a conference abstract [xvi] which is [probably] an observational study and did not report the robot used. All models simulated the treatment effect by a direct decrease in revision rates; however, 3 models applied the effect for only 2 years after surgery and one for 6 years (a more conservative approach to extrapolation of the effect than the models on r-TKR which applied the treatment effect to the entire time horizon).

The inputs for the costs of the robots were derived from NAVIO and MAKO.

Their time horizons ranged from 5 years to a lifetime and used 1-year cycles. The patient populations across these models were all 65 years old. They all included upfront costs for the

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[xiv] Battenberg AK, Netravali NA, Lonner JH. A novel handheld roboticassisted system for unicompartmental knee arthroplasty: surgical technique and early survivorship. J Robot Surg 2020;14(01):55–60
[xv] Kleeblad LJ, Borus TA, Coon TM, et al. Midterm survivorship and patient satisfaction of robotic-arm-assisted medial unicompartmental knee arthroplasty: a multicenter study. J Arthroplasty 2018;33:1719–1726.
[xvi] Conditt M, Coon T, Roche M, et al. "Two Year Survivorship of Robotically Guided Unicompartmental Knee Arthroplasty". Bone Joint J Orthop Proc Suppl 2013;95-B(Suppl. 34):294.

capital acquisition of the robot and assumed a volume of 100 surgeries per year to define the costs per case of the robots. All models explored different caseload thresholds on sensitivity analysis.

5.5.2.2 Results for r-UKR vs. cUKR

The results as reported in the primary studies comparing robot-assisted UKR to conventional UKR are summarized in Table 5-9.

Cost-effectiveness estimates varied widely depending on the willingness-to-pay (WTP) thresholds assumed for adoption and surgical volumes.

From the UK perspective, the ICER per QALY ranged from ₤2,831 with NAVIO (5-year time horizon to ₤1170 with MAKO (lifetime horizon). Robot-assisted UKR with NAVIO seemed dominant (i.e. less costly with better outcomes) when patients are under 55 years old, and over 7 years follow-up; and likely to be cost-effective 100% of the time under a WTP threshold of ₤20,000. Lower surgical volumes highly impact NAVIO cost-effectiveness profile (₤43,581 per QALY if 20 surgeries per year) and threshold analysis estimated the volume needed for the robot costs to break even at >139 UKR/year.

From the USA perspective, the ICER per QALY for MAKO was estimated at $ 47,180 (lifetime horizon). At a WTP threshold of $50,000/QALY the Robot-assisted UKR could be considered cost-effective if (1) case volume exceeded 94 cases per year; (2) the 2-year failure rate was below 1.2% (compared to a 2-year failure rate of 3.1% with conventional UKR); (3) provided an improved failure rate beyond 2 years; (4) present discounted costs of the robot system and maintenance contract lower than <$1.426 million; (5) the robot system lifetime was at least 4.7 years, and (6) average patient age was <67 years.

A threshold analysis, based on ICER per revision avoided, estimated the volume needed for MAKO costs to break even between 221 surgeries (if age 55) and 431 surgeries (if age 65), over 5 years.

Table 5-9 Summary of results from the identified economic studies (per person) – robot-assisted UKR vs. conventional UKR

SR		CADTH 2022 (SR)[34]	Bai et al 2022 (SR)[70] CADTH 2022 (SR)[34]	Bai et al 2022 (SR)[70]
Study	**Yeroushalmi 2022[68]**	**Nehrera et al 2020[69]**	**Clement et al. 2019[66]**	**Moschetti et al 2016[67]**
Robot	NAVIO, Smith & Nephew (Costs and Effects)	NAVIO, Smith & Nephew (Costs and Effects)	MAKO, Stryker (Costs and Effects)	MAKO (Costs), Robot not reported (Effect)
Time Horizon	5 years	5 years	Lifetime	Lifetime
Currency	2018 US$	2017/2018 £	2019 £ (?)	2012 US$
ICER per QALY		High volume (100/y): £2,831 Low volume (20/y): £43,581	£1170	$ 47,180
Value (as a function of WTP and a number of other variables)		The probability of being cost-effective at a WTP of £20,000/QALY is 100% (100 cases/year) ICER/QALY ranged from dominant to £33,704 in OWSA Dominant when patients are under 55 years old, and 7-year follow-up.		r-UKR was cost-effective (WTP = 50,000/QALY) if (1) case volume exceeded 94 cases per year; (2) robot-assisted UKR 2-year failure rate was below 1.2% (compared to a 2-year failure rate of 3.1% with conventional UKR); (3) robot-assisted UKR provided an improved failure rate beyond 2 years; (4) present discounted costs of the robot system and maintenance contract were <$1.426 million; (5) the robot system lifetime was at least 4.7 years; and (6) average patient age was <67 years.

Other cost-effectiveness measures	**ICER per revision avoided (per patient)** 65-year: $14,737 55-year: $7,271 75 years: $28,716 **7-years time horizon:** $2,407 (cost saving afterward) **Threshold Analysis - Volume needed to break even** Age 65-year: 431 patients per year over 5 years Age 55-year: 221 patients per year over 5 years	**Threshold Analysis** – Volume needed to break even = > 139 UKR/year

(?) Currency year not stated, assumed the year of the article submission; SR = systematic review; QALYs=Quality-adjusted life years; ICER=incremental cost-effectiveness ratio; WTP=willigness-to-pay; NR=not reported; UKR = unicompartmental knee replacement; r-UKR = robot-assisted unicompartmental knee replacement; OWSA: one-way sensitivity analysis

5.5.2.3 Results r-UKR vs. cTKR

Cost-effectiveness estimates varied widely depending on surgical volumes and length of stay.

From the UK perspective, the ICER per QALY of robot-assisted UKR with MAKO was estimated at £1395 (2019 £, lifetime horizon) when compared with conventional total knee replacement instead.

This cost-effectiveness profile is highly affected by the savings with patient stay (assumed shorter in UKR vs TKR). "For a high-volume centre performing 200 r-UKRs per year with a mean two-day length of stay, the cost per QALY was £648, which was reduced further to £506 for a single-day stay; for day case, the cost per QALY was £364 relative to TKR (Fig. 3). A centre performing 320 r-UKRs per year as day cases would be cost neutral compared with TKR, with the increased costs of surgery and revision being compensated for by the cost savings of no inpatient stay."

5.5.3 Discussion of findings in the economic studies

5.5.3.1 What is the cost-effectiveness of the technology in the same clinical populations from the previously published economic analysis? Discuss limitations of findings and other aspects relevant to the BC context (if needed).

The cost-effectiveness studies available include only 2 robots (MAKO and NAVIO) of interest for the BC context. However, in some studies, the robot effect is mixed evidence from other robots that are not available for purchase in BC (e.g. ROBODOC and CASPAR). Extrapolating the results between robots requires extra caution.

For **total knee replacements**, the cost-effectiveness of robot-assisted surgery is widely dependent on the WTP threshold, the annual surgical volume of the hospital (assuming costs with the capital acquisition), patient risk profile (e.g. age, BMI, sex) and how much it can reduce revisions. Only one of the five economic studies included the effect of MAKO (from 2 non-RCT studies) and aggregated it to the effects of ROBODOC (from RCT studies)[64]. There is considerable uncertainty in the results and it is challenging to extrapolate these results to the BC context.

For **unicompartmental knee replacements,** the available economic evaluations are all based on clinical evidence from non-RCT studies. They estimated both NAVIO and MAKO as cost-effective but the results are highly variable depending on WTP threshold, surgical volumes and risk of revision related to age.

- Surgical volume: The volume needed for the costs with robots to break even would need to be higher than 139 per year with NAVIO and 221-431 surgeries per year with MAKO. For reference, the hospital in BC with the highest volume of unicompartmental knee replacements [15] performs approximately 86 surgeries per year (which represents 21% of its total number of knee replacements). Even if the two largest hospitals in BC shifted their numbers of total replacements to partial replacements, these volumes would unlikely be achieved.
- Revision rate: MAKO could be considered cost-effective in the US[67] if the 2-year revision rate with robot surgery was below 1.2% compared to 3.1% with conventional partial replacement (a 61% reduction). For reference, the Canadian 2-year revision rate for partial replacement ranges from 3.25% (medial partial

arthroplasty) to 4.65% (lateral partial arthroplasty)[xvii]. Assuming the same 61% reduction by the use of robots, these 2-year revision rates would need to come down to 2-2.8%. The clinical review of RCTs conducted by our team (section 5.4.4) found mixed evidence of revision rates for robotic-assisted surgery.

- Patient age: From the USA perspective, MAKO could be considered cost-effective if the average of patients undergoing partial replacement was <67 years. For reference, in only 8 of the 18 hospitals in BC providing unicompartmental knee replacements is the patient population average age below 67 years; those sites are distributed mostly across the Interior and Northern health authorities (Appendix B) and their volume of partial replacements range from 5-52 surgeries per year. Therefore, it is challenging to extrapolate these cost-effectiveness estimates to the BC context. Essentially only 8 sites in BC have room to shift their volumes to more partial replacements for younger patients (i.e. have both the average age of their patient population undergoing total knee replacement below 67 years of age AND less than 9.5% of their total number of knee replacements already being partial replacements). However, based on those 2 criteria, none of them would achieve 95 partial replacements per year; the only 2 sites that could potentially come closer to this volume threshold would be Surrey

[xvii] Source: Canadian Institute for Health Information. Hip and Knee Replacements in Canada: CJRR Annual Report, 2020–20211.CIHI. Hip and Knee Replacements in Canada: CJRR Annual Report, 2020–2021. Ottawa, ON: 2022. Available at https://www.cihi.ca/sites/default/files/document/hip-knee-replacements-in-canada-cjrr-annual-report-2020-2021-en.pdf.; Fig 13, page 60.

Memorial (with approximately 86 surgeries per year) and Royal Jubilee (with approximately 74 surgeries per year).

Hickey et al[29], as discussed earlier, developed a model that, despite using costs and effects from robots not available in the BC market (ROBODOC and CASPAR), provides a very interesting framework to assess the cost-effectiveness range for adopting these technologies. They incorporate into a microsimulation-Markov model, site-specific aspects such as the risk profile of its patients for revision (age, BMI and sex), caseload and a risk-prioritized policy for the use of robots (i.e. to a proportion of the cases instead of to all cases). This model can estimate the hospital-specific utilization range for adoption outside of which the robots stop being cost-effective. Leveraging the use of this model (reusing and adapting) is worth considering.

Ideally, the cost-effectiveness of the robots should be assessed at the site level (and per robot as they can have very different costs) and take into consideration their combination of patients undergoing partial and total knee replacements altogether as they can share the amortized costs of the same robot but contribute with very different risks of revisions, costs and benefits. Hickey et al model [29] could be adapted to produce a holistic analysis at the hospital level. However, questions remain about whether the existing evidence of the effect of the robots on alignment or revision rates is strong enough to support such analytical efforts (which are not insignificant).

To support decision-making in BC on whether to pursue further analysis, develop alternative risk-sharing strategies, or pragmatic studies to collect more data relevant to the BC knee implant context, we developed a simple analytical tool[xviii] based on achieving cost neutrality. For example, a hospital that performs on average 560 knee replacements per year and sources 99% of its knee implants from Stryker [redacted] if it were to acquire MAKO at the current prices, the robot would have to prevent 88% of the expected revisions following the 10-year after primary surgeries to be cost-neutral. Even in a scenario at zero capital costs (e.g. donations through foundations) but incurring service fees and consumables costs, MAKO would still have to decrease revisions by 71% to offset its costs of adoption. Alternatively, ROSA would have to prevent 53% of the revisions and CORI and VELYS would never reach cost neutrality as they would need to prevent more revisions than possibly expected from this site.

There is a floor effect of how many revisions can be avoided to offset the costs with the new technology. Observational studies have shown that among patients with neutral alignment, there is still a residual 2.7% cumulative rate of revisions over 10 years.[71] Therefore, robot systems along with the costs of their annual services and implants should be priced considering how much "room for improvement" exists in a specific setting. For the same hospital example above, MAKO would need to be offered at zero cost (e.g. capital, annual services, apps, etc.) and disposables would need to be at least 27% cheaper to have a possibility of achieving cost neutrality (given the existing room from improvement), and assuming surgeons would reach the same alignment results as those demonstrated in the clinical trials (at least 95% of patients in neutral alignment).

[xviii] provided as supplementary material to the HTAO

5.6 Overall Conclusion

All the evidence available for review included only 2 of the 5 robots from manufacturers of interest for BC [redacted]

The clinical evidence review of RCT studies shows that robot-assisted knee replacement consistently performed better in alignment when compared with conventional surgery in both UKR and TKR. The evidence on revisions is inconsistent and inconclusive.

It is ambitious to extrapolate the results from the economic evidence review to the BC context as it was based on non-RCT data (despite some evidence existing from RCTs), varies widely depending on WTP, surgical volumes and patients' risk of revision at the site level. The biggest gains seem to be in robotic-assisted UKRs, but based on the hospital-level data for BC, very few hospitals could potentially reach feasible volumes of UKRs to offset the cost of robots unless there is a desire to centralize these surgeries.

A simple analytical tool for use in BC has been developed to explore cost neutral adoption of robots, at the current prices. It shows that, even at zero capital costs, between 40% to 100% reduction in revisions would have to be seen to offset their costs. Robot systems, along with the costs of their annual services and implants, need to be priced considering how much potential for return on investment exists in a specific site.

Given the state of the evidence and the nuances for the BC context, we see four possible approaches to moving forward in relation to the question of robots for knee replacement in the BC context:

1. To build a de novo simulation model specific to the BC context based on the **direct effect on revision rates.** This would require us to expand the literature search focused on revision rates with robotic-assisted surgery in a longer term from non-RCT type studies to include registry data, with the goals of potentially including more robots of interest for BC.
2. To re-use the model from Hickey et al[29] (through collaboration with those researchers) and adapt to the BC context, relying on the assumption that **malalignment indirectly leads to a higher risk of revision** in the longer term. This option can only use the alignment data from the RCTs using MAKO and NAVIO.
3. To discontinue the assessment at this stage and embark on a pragmatic trial assessing clinical and cost outcomes.
4. To discontinue the assessment and consider early monitored adoption in certain sites aiming for cost-neutral implementation, using the simple analytical tool (presented above) to assess site-specific feasibility relative to surgical volumes, revision rates and need for shift in implant market share.

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[redacted]

Appendix E Search Strategies

Robotic Knee Arthroscopy

Final Strategy

2022 Dec 21

Ovid Multifile

Database: Embase <1974 to 2022 December 20>, EBM Reviews - Cochrane Central Register of Controlled Trials <November 2022>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to December 14, 2022>, Ovid MEDLINE(R) ALL <1946 to December 19, 2022>

Search Strategy:

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1 ((Mako$2 or ROSA$2 or CORI$2) adj10 (arthroscop* or arthro-scop* or robot* or surg* or system$2 or PKA or TKA or UKA)).tw,kw,kf. (1858)

2 Robotic Surgical procedures/ (33846)

3 (robot* adj3 (aided or arthroplas* or arthro-plast* or assist* or procedur* or surg*)).tw,kw,kf. (85954)

4 (robot* adj3 (device? or platform? or system?)).tw,kw,kf. (30095)

5 or/2-4 [ROBOTIC SURGERY] (110359)

6 Arthroplasty, Replacement/ (8937)

7 (arthroplast* or arthro-plast*).tw,kw,kf. (192223)

8 (joint? adj3 (arthroplas* or arthro-plast* or replac*)).tw,kw,kf. (40805)

9 (replacement adj1 (arthroplast* or arthro-plast*)).tw,kw,kf. (4755)

10 or/6-9 [ARTHROPLASTY] (212090)

11 5 and 10 [ROBOTIC SURGERY - ARTHROPLASTY] (1955)

12 Knee/ (89587)

13 exp Knee Joint/ (147082)

14 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ti,kw,kf. (253039)

15 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ab. /freq=2 (250645)

16 or/12-15 [KNEES] (390284)

17 11 and 16 [ROBOTIC SURGERY/ARTHROPLASTY - KNEES] (1369)

18 Arthroplasty, Replacement, Knee/ (39255)

19 ((arthroplast* or arthro-plast*) adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (77981)

20 (replac* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (35378)

21 (reconstruct* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (10191)

22 (PKA or TKA or UKA).ti,kw,kf. (19093)

23 ((PKA or TKA or UKA) adj10 (arthroscop* or knee? or kneecap?)).ab. (32203)

24 or/18-23 [KNEE ARTHROPLASTY] (129406)

25 5 and 24 [ROBOTIC KNEE ARTHROPLASTY] (1670)

26 1 or 17 or 25 [ROBOTIC KNEE ARTHROPLASTY] (3352)

27 exp Animals/ not Humans/ (16588693)

28 26 not 27 [ANIMAL-ONLY REMOVED] (2784)

29 (comment or editorial or news or newspaper article or (letter not (letter and randomized controlled trial))).pt. (4342484)

30 28 not 29 [OPINION PIECES REMOVED] (2713)

31 2022*.dt. (1547867)

32 30 and 31 [UPDATE DATES] (230)

33 limit 30 to yr="2022-current" (572)

34 32 or 33 [UPDATE DATE OR PUBLICATION 2022-PRESENT] (581)

35 34 use medall [MEDLINE RESULTS] (280)

36 ((Mako$2 or ROSA$2 or CORI$2) adj10 (arthroscop* or arthro-scop* or robot* or surg* or system$2 or PKA or TKA or UKA)).dv,tw,kw,kf. (1955)

37 robot assisted surgery/ (34901)

38 (robot* adj3 (aided or arthroplas* or arthro-plast* or assist* or procedur* or surg*)).tw,kw,kf. (85954)

39 (robot* adj3 (device? or platform? or system?)).tw,kw,kf. (30095)

40 or/37-39 [ROBOTIC SURGERY] (110615)

41 replacement arthroplasty/ (8937)

42 (arthroplast* or arthro-plast*).tw,kw,kf. (192223)

43 (joint? adj3 (arthroplas* or arthro-plast* or replac*)).tw,kw,kf. (40805)

44 (replacement adj1 (arthroplast* or arthro-plast*)).tw,kw,kf. (4755)

45 or/41-44 [ARTHROPLASTY] (212091)

46 40 and 45 [ROBOTIC SURGERY - ARTHROPLASTY] (1958)

47 knee/ (89587)

48 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ti,kw,kf. (253039)

49 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ab. /freq=2 (250645)

50 or/47-49 [KNEES] (371427)

51 46 and 50 [ROBOTIC SURGERY/ARTHROPLASTY - KNEES] (1367)

52 knee arthroplasty/ (50523)

53 exp knee replacement/ (22465)

54 ((arthroplast* or arthro-plast*) adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (77981)

55 (replac* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (35378)

56 (reconstruct* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).tw,kw,kf. (10191)

57 (PKA or TKA or UKA).ti,kw,kf. (19093)

58 ((PKA or TKA or UKA) adj10 (arthroscop* or knee? or kneecap?)).ab. (32203)

59 or/52-58 [KNEE ARTHROPLASTY] (135581)

60 40 and 59 [ROBOTIC KNEE ARTHROPLASTY] (1706)

61 36 or 51 or 60 [ROBOTIC KNEE ARTHROPLASTY] (3447)

62 (exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/) not (exp human/ or exp human experimentation/ or exp human experiment/) (12140017)

63 61 not 62 [ANIMAL-ONLY REMOVED] (3202)

64 editorial.pt. or (letter.pt. not randomized controlled trial/) (3833336)

65 63 not 64 [OPINION PIECES REMOVED] (3117)

66 conference abstract.pt. (4625819)

67 65 not 66 [CONFERENCE ABSTRACTS REMOVED] (2777)

68 2022*.dc. (2378381)

69 67 and 68 [UPDATE DATES] (298)

70 limit 67 to yr="2022-current" (561)

71 69 or 70 [UPDATE DATE OR PUBLICATION 2022-PRESENT] (607)

72 71 use oemezd [EMBASE RECORDS] (309)

73 ((Mako$2 or ROSA$2 or CORI$2) adj10 (arthroscop* or arthro-scop* or robot* or surg* or system$2 or PKA or TKA or UKA)).ti,ab,kw. (1800)

74 Robotic Surgical procedures/ (33846)

75 (robot* adj3 (aided or arthroplas* or arthro-plast* or assist* or procedur* or surg*)).ti,ab,kw. (83020)

76 (robot* adj3 (device? or platform? or system?)).ti,ab,kw. (29677)

77 or/74-76 [ROBOTIC SURGERY] (108579)

78 Arthroplasty, Replacement/ (8937)

79 (arthroplast* or arthro-plast*).ti,ab,kw. (187809)

80 (joint? adj3 (arthroplas* or arthro-plast* or replac*)).ti,ab,kw. (39018)

81 (replacement adj1 (arthroplast* or arthro-plast*)).ti,ab,kw. (3313)

82 or/78-81 [ARTHROPLASTY] (207556)

83 77 and 82 [ROBOTIC SURGERY - ARTHROPLASTY] (1909)

84 Knee/ (89587)

85 exp Knee Joint/ (147082)

86 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ti,kw. (241302)

87 (knee or knees or kneecap? or patella* or patellofemoral* or patello-femoral*).ab. /freq=2 (250645)

88 or/84-87 [KNEES] (385438)

89 83 and 88 [ROBOTIC SURGERY/ARTHROPLASTY - KNEES] (1322)

90 Arthroplasty, Replacement, Knee/ (39255)

91 ((arthroplast* or arthro-plast*) adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).ti,ab,kw. (75904)

92 (replac* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).ti,ab,kw. (32850)

93 (reconstruct* adj3 (knee or knees or knee cap? or patella* or patellofemoral* or patello-femoral*)).ti,ab,kw. (10090)

94 (PKA or TKA or UKA).ti,kw. (16423)

95 ((PKA or TKA or UKA) adj10 (arthroscop* or knee? or kneecap?)).ab. (32203)

96 or/90-95 [KNEE ARTHROPLASTY] (126640)

97 77 and 96 [ROBOTIC KNEE ARTHROPLASTY] (1639)

98 73 or 89 or 97 [ROBOTIC KNEE ARTHROPLASTY] (3266)

99 conference proceeding.pt. (214308)

100 98 not 99 [CONFERENCE PROCEEDINGS REMOVED] (3248)

101 limit 100 to yr="2022-current" (580)

102 2022*.up. (7440341)

103 100 and 102 (910)

104 101 or 103 [UPDATE LIMIT APPLIED] (913)

105 104 use coch,cctr [COCHRANE RECORDS] (172)

106 35 or 72 or 105 [ALL DATABASES] (761)

107 remove duplicates from 106 (510) [TOTAL UNIQUE RECORDS]

108 107 use medall [MEDLINE UNIQUE RECORDS] (278)

109 107 use oemezd [EMBASE UNIQUE RECORDS] (80)

110 107 use coch [CDSR UNIQUE RESULTS] (0)

111 107 use cctr [CENTRAL UNIQUE RESULTS] (152)

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Appendix F **List of excluded studies**

F.1 Suggested studies by clinical experts

AUTHOR	YEAR	TITLE	JOURNAL	VOLUME	ISSUE	PAGES	ABSTRACT DECISION	ABSTRACT COMMENT
Arthur L Malkani 1, Martin W Roche 2, Frank R Kolisek 3, Kenneth A Gustke 4, William J Hozack 5, Nipun Sodhi 6, Alexander Acuña 7, Rushabh Vakharia 2, Hytham S Salem 8, Charles Jaggard 3, Langan Smith 9, Michael A Mont 8	2020	New Technology for Total Knee Arthroplasty Provides Excellent Patient-Reported Outcomes: A Minimum Two-Year Analysis	Surg Technol Int	36		276-280	Exclude	One-arm (robot) observational study (no comparator, n= 188), 2-year follow-up of PROMS
James D Sires 1, Johnathan D Craik 2, Christopher J Wilson 2	2021	Accuracy of Bone Resection in MAKO Total Knee Robotic-Assisted Surgery	J Knee Surg	34	7	745-748. doi: 10.1055/s-0039-1700570. Epub 2019 Nov 6.	Exclude	One-arm (robot) observational study (no comparator, n= 45), alignment pre and post planning
Joshua A. Lawson, MD1 Andrew T. Garber, MD1 Jeffrey D. Stimac, MD2 Rama Ramakrishnan, MS, MBA3 Langan S. Smith, BS2 Arthur L. Malkani, MD1	2019	Does Robotic-Assisted Total Hip Arthroplasty Improve Accuracy of Cup Positioning?					Exclude	Hip replacement - out of scope
Wataru Ando1 & Masaki Takao2 & Hidetoshi Hamada2 &	2021	Comparison of the accuracy of the cup position and					Exclude	Hip replacement - out of scope

Keisuke Uemura1 & Nobuhiko Sugano1		orientation in total hip arthroplasty for osteoarthritis secondary to developmental dysplasia of the hip between the Mako robotic arm-assisted system and computed tomography-based navigation						
Emily L. Hampp, PhD1 Morad Chughtai, MD2 Laura Y. Scholl, MS1 Nipun Sodhi, BA3 Manoshi Bhowmik-Stoker, PhD1 David J. Jacofsky, MD4 Michael A. Mont, MD3	2019	Robotic-Arm Assisted Total Knee Arthroplasty Demonstrated Greater Accuracy and Precision to Plan Compared with Manual Techniques					Exclude	Cadaver study
Tsung-Yuan Tsai, PhD a, Dimitris Dimitriou, MD a, Ming Han Lincoln Liow, MD a, b, Harry E. Rubash, MD a, Guoan Li, PhD a, Young-Min Kwon, MD, PhD a,	2016	Three-Dimensional Imaging Analysis of Unicompartmental Knee Arthroplasty Evaluated in Standing Position: Component Alignment and In Vivo Articular Contact	The Journal of Arthroplasty	31		1096e1101	Exclude	One-arm sutdy (not robot) of implants alignment on image (X-Ray). No comparator
Jack Cramer1, David Fulker1	?	The use of CT-based robotic arm-assisted total knee arthroplasty is associated with a					Exclude	Adhoc report by Stryker. Not published in any peer-reviewed journal. Gavin ?

		reduced rate of revision: An analysis of procedures from the Australian Orthopaedic Association National Joint Replacement Registry						maybe if you are going into registry data for revison rates - 7 years follow up
B. Kayani, S. Konan, J. Tahmassebi, J. R. T. Pietrzak, F. S. Haddad	2018	Robotic-arm assisted total knee arthroplasty is associated with improved early functional recovery and reduced time to hospital discharge compared with conventional jig-based total knee arthroplasty	THE BONE & JOINT JOURNAL	100	B	930-7	Exclude	Comparative consecutive cohort study (non-RCT, n=80, one surgeon). Measured pain, analgesia, hemoglobin levels, time to straight leg, physiotherapy sessions, and knee flexion at discharge. Gavin?
David R. Maldonado, MD Cammille C. Go, BS Cynthia Kyin, BA Philip J. Rosinsky, MD Jacob Shapira, MD Ajay C. Lall, MD, MS Benjamin G. Domb, MD	2020	Robotic Arm-assisted Total Hip Arthroplasty is More Cost-Effective Than Manual Total Hip Arthroplasty: A Markov Model Analysis					Exclude	Hip replacement - out of scope
S.J. Bhimani, R. Bhimani, A. Smith, C. Eccles, L. Smith, A. Malkani	2020	Robotic-assisted total knee arthroplasty demonstrates decreased postoperative pain and opioid	Bone Joint Open			8–12.	Exclude	Retrospective study. Gavin

		usage compared with conventional total knee arthroplasty					
Austin F. Smith, MD1 Christian J. Eccles, MD1 Samrath J. Bhimani, MD1 Kevin M. Denehy, MD1 Rohat B. Bhimani, BA2 Langan S. Smith, BS3 Arthur L. Malkani, MD4	2021	Improved Patient Satisfaction following Robotic-Assisted Total Knee Arthroplasty	J Knee Surg	34	730–738.	Exclude	Comparative consecutive cohort study (non-RCT, n=223, 1 year follow-up). Measured patient staisfaction. Gavin?
Anton Khlopas, MD1 Nipun Sodhi, MD2 William J. Hozack, MD3 Antonia F. Chen, MD, MBA4 Ormonde M. Mahoney, MD5 Tracy Kinsey, MSPH5 Fabio Orozco, MD2 Michael A. Mont, MD1,2	2020	Patient-Reported Functional and Satisfaction Outcomes after Robotic-Arm-Assisted Total Knee Arthroplasty: Early Results of a Prospective Multicenter Investigation	J Knee Surg	33	685–690.	Exclude	252 patients (102 manual and 150 robot-assisted) were enrolled into a prospective, nonrandomized, open-label, multicenter comparative cohort study. Measured functional scores, patients symptoms and satisfaction. Follow up 3 months
Babar Kayani, MRCS, MBBS, BSc (Hons) a, b, *, Sujith Konan, MBBS, MD (Res), FRCS (Tr & Orth) a, b, Jurek R.T. Pietrzak, MB BCh, FCS(SA)Orth	2018	Iatrogenic Bone and Soft Tissue Trauma in Robotic-Arm Assisted Total Knee Arthroplasty Compared With Conventional Jig-	The Journal of Arthroplasty	33	2496e2501	Exclude	Comparative consecutive cohort study (non-RCT, n=60). Measured soft tissue injury, MASTI scores. Gavin?

a, b, Fares S. Haddad, FRCS (Ed), Dip Sports Med, FFSEM a, b		Based Total Knee Arthroplasty: A Prospective Cohort Study and Validation of a New Classification System						
N. Ng, P. Gaston, P. M. Simpson, G. J. Macpherson, J. T. Patton, N. D. Clement	2021	Robotic arm-assisted versus manual total hip arthroplasty	Bone Joint J	6	103-B	1009–1020.	Exclude	Hip replacement - out of scope
MAKO		The clinical and economic value of Mako SmartRobotics					Exclude	White paper produced by MAKO. We are not going to dissect this type of paper to separate each article mentioned within.
N. D. Clement, A. Bell, P. Simpson, G. Macpherson, J. T. Patton, D. F. Hamilton	2020	Robotic-assisted unicompartmental knee arthroplasty has a greater early functional outcome when compared with manual total knee arthroplasty for isolated medial compartment arthritis	Bone Joint Res	9	1	15–22	Exclude	Comparative consecutive cohort study (non-RCT, n=120, 30 at the robot arm). Measured OKS, EQ5D, FJS, patient satisfaction, LOS. 6 months follow up
N. D. Clement, P. Gaston, A. Bell, P. Simpson, G. Macpherson,	2021	Robotic arm-assisted versus manual total hip arthroplasty	Bone Joint Res	10	1	22–30.	Exclude	Hip replacement - out of scope

D. F. Hamilton, J. T. Patton							
Chen, Z., Bonutti, P.M., Barsoum, W.K., Mont, M.A., Bains, S.S. and Jacofsky, D.J.	2022	Technology Review: CT Scan-Guided, 3-Dimensional, Robotic-Arm Assisted Lower Extremity Arthroplasty	Surgical Technology International	40	297-308	Exclude	Technology review, crossreferenced
Gregory, D.A., Coppolecchia, A., Scotti, D.J., Chen, Z., Mont, M.A. and Jacofsky, D.	2022	A 90-Day Episode-of-Care Analysis Including Computed Tomography Scans of Robotic-Arm Assisted versus Manual Total Knee Arthroplasty	The Journal of Knee Surgery	11	11	Exclude	Cost comparison, Robot unclear, summary of other cost studies and models in discussion
Christina L Cool 1, David J Jacofsky 2, Kelly A Seeger 1, Nipun Sodhi 3, Michael A Mont 3	2019	A 90-day episode-of-care cost analysis of robotic-arm assisted total knee arthroplasty	J Comp Eff Res	5	327-336	Exclude	Cost comparison, MAKO. Observational 90-day EOC costs
Gregory S. Kazarian, AB, Jess H. Lonner, MD, Mitchell G. Maltenfort, PhD, Hassan M.K. Ghomrawi, PhD, MPH, and Antonia F. Chen, MD, MBA	2018	Cost-Effectiveness of Surgical and Nonsurgical Treatments for Unicompartmental Knee Arthritis	J Bone Joint Surg Am.		1653-60	Exclude	Compared TKR vs UKR but not the ROBOT effect, just the technical approach per se
Michael A. Mont, MD1 Christina Cool, MPH2 David Gregory, MPA, FACHE2 Andrea Coppolecchia,	2021	Health Care Utilization and Payer Cost Analysis of Robotic Arm Assisted Total Knee	J Knee Surg	34	328–337.	Exclude	Cost comparison, MAKO. Observational. Index cost, discharge, 3--day,

MPH3 Nipun Sodhi, MD1 David J. Jacofsky, MD4	Arthroplasty at 30, 60, and 90 Days		60-day, 90-day EOC costs, post op utilization, readmissions

Appendix G Description of the included studies

Please see attached excel file.

Appendix H **Critical appraisal of included clinical studies**

Study name \ Outcomes	Robot type	Intervention	Comparator	Intervention sample size	Comparator sample size	Critical apprasial					
Domain						Random sequence generation	Allocation concealment	Blinding of investigators and participants	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective outcome reporting (reporting bias)
Banger 2020/ Blyth 2021/ Banger 2022	MAKO	RA-biUKA	cTKA	38	42	Some concern	High	High	High	Low	Low
Vaidya 2022	NAVIO	RA-TKA	cTKA	32	28	Low	High	High	High	Low	Low
Bell 2016/Blyth 2017/ Montesharei 2018/Gilmour 2018/Banger 2021	MAKO	RA-UKA	cUKA	70	69	Low	High	Low	High	High	Low
Batailler 2022	NAVIO	RA-UKA	cUKA	33	33	Low	High	High	High	Low	Low
Kayani 2021	MAKO	RA-TKA	cTKA	15	15	Low	High	High	Low	Low	Low
Thiengwittayaporn 2022	NAVIO	RA-TKA	cTKA	77	77	Low	High	High	High	Low	Low

Appendix I Overview of the economic studies' characteristics and analytic approach - for robot-assisted TKR

Systematic Review	
Primary Study	**Hickey et al 2023[29]**
Robot	**ROBODOC+CASPAR (Costs and Effects)**
Policy questions/Aim	(1) Given key demographic parameters characterizing a patient population, together with estimates of the precision achievable with selected forms of technology assistance in TKR, can we estimate the expected distributions of anticipated reductions in lifetime revision risk for that population and the associated improvements in quality-adjusted life years (QALYs) that would be expected to result? (2) Are there realistic practice characteristics (such as combinations of local patient demographics and capital and per-procedure costs) for which applying a per-patient risk-prioritized policy for using technology-assisted TKR could be considered cost-effective based on projected cost savings from reductions in revision rates?
Funding	Centre for Hip Health and Mobility + Natural Sciences and Engineering Research Council. Two of the authors have COIs
Type	Cost-utility / Threshold analysis
Target Population	Patients submitted to TKR - categorized with low or elevated intrinsic risk of revision (based on age, BMI and gender)
Interventions	Robot-assisted (1), Patient-specific instrumentation (PSI, 2), Navigation (3), and Hypothetical ideal-TKR technology (4) that could deliver perfect overall coronal alignment
Comparator	Conventional TKR
Analytic Method	Probabilistic
Modelling	Microsimulation-Markov
Effectiveness	The baseline implant survival rate used to simulate TKR patients was selected to be 93% at 15 years as estimated from a review of national joint replacement registry reports from Australia and Finland The treatment effect was modelled indirectly in terms of revision risk associated with 3 categories of coronal alignment (vagus, varus and neutral, observational data (n=982, Lee 2018[xix])); The effect of the technologies was modelled directly in enabling those alignments compared with conventional surgery (PSI and Navigation based on an NMA; Robots based on a SR with metanalysis, Ren Y 2019 – 6 RCT ROBODOC+CASPAR, 1 Cohort Study ROBODOC). Assumed only 1 revision over the time horizon.
Country	USA
Perspective	Payer perspective
Time Horizon	20 years
Discount Rate (Costs & Outcomes)	0%
Cycle length	1-year
Reported Outcomes	QALYs, reductions in the lifetime risk of revision, costs

[xix] Lee BS, Cho HI, Bin S il, Kim JM, Jo BK. Femoral component varus malposition is associated with tibial aseptic loosening after TKA. Clin Orthop Relat Res. 2018;476:400-407

Resource Use and Costs	Costing informed from an extensive literature review adjusted for inflation and currency to 2021 USD; costing categories included, revision costs, fixed and variables costs only directly related to the assistive technologies (disposables, medical imaging, operating room time, and reprocessing). Not other costs related to the episode of care or the implant costs were included.
Uncertainty/ Sensitivity analysis	Scenario analyses as a function of the percentage of patients treated with the technologies were presented as a sensitivity analysis.
Systematic Review	
Primary Study	**Hua et al 2022[63]**
Robot	**MAKO (Costs)/ROBODOC (effects)**
Policy questions/Aim	Expand on previous cost-effectiveness of robotic-arm assisted TKR in the Medicare-aged population with knee OA including exploring the impact of hospital volume on cost-effectiveness outcomes.
Funding	No external funding. All authors declared no COI
Type	Cost-utility
Target Population	Medicare beneficiaries aged 65 years undergoing treatment for end-stage knee OA in hospitals with an annual volume of 50 procedures
Interventions	Robot-assisted TKR
Comparator	Conventional TKR
Analytic Method	Deterministic
Modelling	Markov model
Effectiveness	The treatment effect of the technology was modelled directly by different annual probability of revision: for the robot-assisted arm at 0.28% (estimates from a 10-year follow-up retrospective study on 71 robot-assisted TKRs ROBODOC) and conventional TKR at 0.49% (from a systematic review on 124 studies). QALY weights, perioperative mortality rates, and following the initial TKR were assumed to be the same regardless of the use of robot assistance. The disutility of having revision surgery was set at 0.1 Assumed only 1 revision over the time horizon.
Country	USA
Perspective	Payer perspective
Time Horizon	10 years
Discount Rate (Costs & Outcomes)	3%
Cycle length	1-year
Reported Outcomes	Total QALYs, total costs, the incremental cost-effectiveness ratio (ICER), and incremental net monetary benefits (INMB)
Resource Use and Costs	Considered 90-day episode-of-care (EOC) costs from a healthcare sector perspective, including intraoperative, inpatient, postoperative costs. Robot system and associated costs from academic institution with a volume of 600 robotic cases annually. The initial purchase costs of $1.3 million was depreciated over a expected 10-year lifetime. Fixed costs, including annual maintenance fees, were summed and divided over annual TKR cases plus disposable costs per case. Other costs that occurred during the episode of care were estimated using Medicare Inpatient Prospective Payment data.
Uncertainty/ Sensitivity analysis	Probabilistic and deterministic sensitivity analysis (included perioperative mortality rates, revision rates, QALYs, and specific components of 90-day EOC costs.)
Systematic Review	CADTH 2022 [34]
Primary Study	**Rajan et al 2022[64]**
Robot	**UNCLEAR (Costs) / ROBODOC+ MAKO (effects)**

Policy questions/Aim	To investigate the cost-effectiveness of robot-assisted TKR versus conventional TKR in patients with knee osteoarthritis.
Funding	NR. Some authors have some industry COI
Type	Cost-utility
Target Population	Patients aged 60 years with advanced knee degenerative joint disease treated with TKR
Interventions	Robot-assisted TKR
Comparator	Conventional TKR
Analytic Method	Deterministic
Modelling	Markov model
Effectiveness	Treatment effect was modelled directly in terms of probability of revision from different sources: - Conventional TKR - 0.78% (<=1 year) and 1.5% (> 1 year) [from 72 RCTs, prospective and retrospective studies from 2009 to 2019] - r-TKR - 0.3% (<=1 year) and 0.6% (> 1 year) [3 RCTs ROBODOC, and observational prospective and retrospective studies -> 4 ROBODOC, 2 MAKO, 1 unclear] Assumed only 1 revision over the time horizon. Utility data: from similar cost-effectiveness studies. QOLs of all revisions the same in both arms BUT QOL of optimal TKR different between study arms. - Conventional TKR - 0.82610 (1 year) and 0.84010 (thereafter) [Tufts University Cost-Effectiveness Analysis Registry from 2006 to 2020] - r-TKR - 0.7644,28 (1 year) and 0.8574 (thereafter) [converted optimal QOL values from published SF-36 functional scores from 1 RCT (n=60) that used ROBODOC]
Country	USA
Perspective	Payer perspective
Time Horizon	Lifetime
Discount Rate (Costs & Outcomes)	3%
Cycle length	1-year
Reported Outcomes	QALYs, costs
Resource Use and Costs	Cost: Medicare reimbursement schedules Fixed cost of robotic surgery included upfront acquisitional capital costs + per case usage costs (disposables + CT scan). Divided by the expected institutional cost (up to 25 TKR/year; 26-200 TKRs/year; and >200 TKRs per year)
Uncertainty/ Sensitivity analysis	Probabilistic and deterministic sensitivity analysis Threshold analysis to determine the annualized per case robotic costs to determine the number needed to treat for a robot-assisted TKR to be cost-effective to an institution.
Systematic Review	CADTH 2022 [34]
Primary Study	**Vermue et al 2021[64]**
Robot	**MAKO (Cost) / ROBODOC+CASPAR (Effects)**
Policy questions/Aim	To provide a preliminary cost-effectiveness analysis of robot-assisted total knee replacement compared with the conventional technique.
Funding	Research Foundation Flanders (FWO) - Belgium
Type	Cost-utility
Target Population	Average patients aged 67 years with end-stage osteoarthritis treated with TKR on a centre with a volume of 70 TKRs/year
Interventions	Robot-assisted TKR
Comparator	Conventional TKR
Analytic Method	Deterministic
Modelling	Markov model

Effectiveness	The treatment effect was modelled based indirectly on revision rates based on direct effect of the technology on alignment. Assumed knee malalignment leads to equally increased revision for r-TKR and TKR A mean outlier rate of malalignment was recorded of 7.2% (SD 5.3) and 25.4% (SD 7.4) for robot-assisted and conventional TKR, respectively (2 RCT ROBODOC, 3 retrospective studies ROBODOC, 1 Cohort comparison (non-RCT) CASPAR) Assumed only 1 revision over the time horizon Yearly revision rates for both neutral mechanical alignment and malalignment were estimated from the incidence of revision surgery in the study of Fang et al. Revision rates at 6.6 years follow-up were normalized to yearly revision rates based on a linear assumption. At 20-years of follow-up, these values are comparable to those available in current literature. Utility data: 0.725 for primary TKR and 0.707 for revision TKR Slover et al., 2006. Assumed the same in both TKR and r-TKR arms. The disutility of having a primary TKR was set at -0.1 in the year following surgery, and -0.15 for aseptic revision and -0.2 for septic revision the year following revision surgery.
Country	USA (mistakenly stated as Belgium by CADTH)
Perspective	Payer perspective
Time Horizon	20 years
Discount Rate (Costs & Outcomes)	3%
Cycle length	1-year
Reported Outcomes	QALYs, costs
Resource Use and Costs	Cost: Ferket et al., 2017 for TKR and revision TKR costs. Robot costs from Manufacturer (Stryker, USA) including CT scan
Uncertainty/ Sensitivity analysis	Probabilistic and deterministic sensitivity analysis (costs. Revision rates, death rate, and utility)
Systematic Review	CADTH 2022[34]
Primary Study	**Burn et al 2020[65]**
Robot	**Not specific to a single ROBOT (threshold analysis)**
Policy questions/Aim	To estimate threshold prices for potential improvements in both quality of life after surgery and reductions in the revision risk after knee and hip replacement from the use of computer- and robot-assisted systems.
Funding	National Institute for Health Research
Type	Cost-utility / Threshold analysis
Target Population	Average profile of patients undergoing knee and hip replacements (71 years old, female, BMI 30) individuals undergoing knee and hip replacements in the UK.
Interventions	Robot-assisted TKR
Comparator	Conventional TKR
Analytic Method	Deterministic
Modelling	Markov model
Effectiveness	Clinical and Cost: the NHS - Clinical (revision and death) practice data link (CPRD - 18 years of data), hospital episode statistics admitted patient care (HES APC) Lifetime risk of revision was estimated to be 5.8% after knee replacement. Utility: the NHS - CPRD HES patient-reported outcome measures (HES PROMS, EQ5D-3L routinely collected before surgery and 6 months after) Pre-op: 0.52. QOL increases over 6 months post-op to 0.82 QOL remains unchanged for patients not requiring revision Revised state is 75% QOL vs unrevised Assumed only 1 revision over the time horizon

	The potential gains from improvements in the effectiveness of surgery were assessed by rerunning the analysis for given improvements in the risk of revision (up to a 50% relative reduction) and quality of life after surgery if unrevised (up to a 5% relative improvement).
Country	UK
Perspective	Payer perspective
Time Horizon	Lifetime
Discount Rate (Costs & Outcomes)	3.50%
Cycle length	1-year
Reported Outcomes	QALYs, costs
Resource Use and Costs	Cost: the NHS - Clinical practice data link (CPRD - 18 years of data), hospital episode statistics admitted patient care (HES APC) Calculated the average costs of conventional surgery. Estimated the threshold for incremental costs of robots to be considered cost-effective
Uncertainty/ Sensitivity analysis	Probabilistic and deterministic threshold analysis (QALYs, Revision rates) Threshold analysis to determine the annualized per case robotic costs to determine the number needed to treat for a robot-assisted TKR to be cost-effective to an institution.

NMA= Network meta-analysis; QALYs=Quality-adjusted life years; NR=not reported; INMB= incremental net monetary benefits; MCER=marginal cost-effectiveness ratio; ICER=incremental cost-effectiveness ratio; NIHR= National Institute for Health Research

Appendix J Overview of the economic studies' characteristics and analytic approach - for robot-assisted UKR

Systematic Review	
Primary Study	**Yeroushalmi et al 2022[68]**
Robot	**NAVIO, Smith & Nephew (Costs and Effects)**
Policy questions/Aim	To evaluate the mid-term cost-effectiveness of r-UKR when compared with that of t-UKR
Funding	Funded by Smith & Nephew
Type	Cost-effectiveness (per revision avoided)
Target Population	Patients with a mean age of 65 years (males and females) having surgery at a high-volume centre (100 UKR/year)
Interventions	r-UKR (robot-assisted unicompartimental KA)
Comparator	tUKR (conventional unicompartimental KA)
Analytic Method	Deterministic
Modelling	Markov model
Effectiveness	Treatment effect was modelled directly in terms of revision rates tUKR: 5-year revision rates from NJR (UK) registry r-UKR: HR calculated to be 0.20 (95% CI: 0.17–0.24, $p < 0.05$, from retrospective multicenter, cohort study with follow-up for 2.3 years, n= 128 NAVIO). The HR was applied only for the first 2 years, after which we assumed the revision rates of r-UKR to be similar to that of t-UKR. Assumed a maximum of 2 revisions over the time horizon. Assumed patients will be converted to TKR at the re-revision (if not yet converted to TKR in the first revision)
Country	USA
Perspective	Payer perspective
Time Horizon	5 years
Discount Rate (Costs & Outcomes)	3%
Cycle length	1-year
Reported Outcomes	N. Revisions, costs
Resource Use and Costs	Cost based on NAVIO capital cost of acquisition and annual service fee + disposables. Amortized by a volume of 100 UKR/year, and an equipment lifespan of 5 years
Uncertainty/ Sensitivity analysis	1-way SA and structural SAs (change in assumptions: such as age, volume of cases seen, and time horizon)
Systematic Review	CADTH 2022[34]
Primary Study	**Nehrera et al 2020[69]**
Robot	**NAVIO, Smith & Nephew (Costs and Effects)**
Policy questions/Aim	Evaluating the cost-effectiveness of non-CT r-UKR when compared with that of t-UKR in the UK.
Funding	NR. All authors are employed by S&N (COI)
Type	Cost-utility
Target Population	Patients aged 65 years eligible for UKR; Also considered patients aged < 55 years, 65 - 74 years, and > 75 years

Interventions	non-CT r-UKR
Comparator	UKR
Analytic Method	Deterministic
Modelling	Markov model
Effectiveness	Treatment effect was modelled directly in terms of revision rates Annual revision probability of UKR = 1.19%, from British National Joint Registry, Annual revision of non-CT r-UKR = HR 0.20 (95% CI: 0.17 to 0.24), from retrospective multicenter, cohort study with follow-up for 2.3 years, n= 128 NAVIO Impact of revisions was limited to two years, after which it was the same in both groups. Assumed a maximum of 2 revisions over the time horizon in which the re-revision is a TKR Equivalent mortality between interventions Utility: Moschetti et al., 2016 - Postsurgery 0.750, Revision 0.565, Re-revision 0.4630
Country	UK
Perspective	Payer perspective
Time Horizon	5 years
Discount Rate (Costs & Outcomes)	3.50%
Cycle length	1-year
Reported Outcomes	QALYs, costs, n. revisions
Resource Use and Costs	Cost: NHS reference cost in 2018/2019 Annual equivalent costs were divided by the expected case volume of 100 cases per year
Uncertainty/ Sensitivity analysis	Probabilistic, deterministic and structural sensitivity analysis Threshold analysis to determine the annualized per case robotic costs to determine the number needed to treat for a robot-assisted TKR to be cost-effective to an institution.
Systematic Review	Bai et al 2022[70]; CADTH 2022[34]
Primary Study	**Clement et al. 2019[66]**
Robot	**MAKO, Stryker (Costs and Effects)**
Policy questions/Aim	Identify the cost per QALY of r-UKR relative to manual TKR and UKR for patients with isolated medial compartment OA of the knee. Secondary aims were to assess whether case volume influences the overall cost and cost per QALY, whether robotic surgery exceeds current United Kingdom willingness to pay cost thresholds, and whether shorter length of hospital stay influences the relative cost per QALY.
Funding	NR. All authors have COIs
Type	Cost-utility
Target Population	Patients with isolated medial compartment OA of the knee, mean age 65y
Interventions	r-UKR (robot-assisted partial KA)
Comparator	tUKR (conventional partial KA) and tTKR (conventional total KA)
Analytic Method	Deterministic
Modelling	Decision-tree + Markov model
Effectiveness	Treatment effect was modelled directly in terms of revision rates Revision/y of r-UKR = 0.5% (prospective, multicentre observational study, n=528 r-UKRs -> MAKO). After the first six years, the annual failure rate for an r-UKR was set at that observed after manual UKR (1.1%) Revision/y of UKR = 1.1%, NJR report Revision/y of TKR = 0.3%, NJR report Assumed only 1 revision over the time horizon
Country	UK
Perspective	NR

Time Horizon	Lifetime
Discount Rate (Costs & Outcomes)	NR
Cycle length	1-year
Reported Outcomes	QALYs, costs
Resource Use and Costs	Cost based on MAKO's 1-year lease costs from vendors, amortized over 100 cases per year
Uncertainty/ Sensitivity analysis	Sensitivity analysis for different thresholds of volume and LOS
Systematic Review	Bai et al 2022[70]
Primary Study	**Moschetti et al 2016[67]**
Robot	**MAKO (Costs), Robot not reported (Effect)**
Policy questions/Aim	To delineate the case volume, revision rates, and costs of the robotic system that are necessary for it to be cost-effective in arthroplasty centers.
Funding	One of the authors has COI
Type	Cost-utility
Target Population	Patients aged 65 undergoing UKR for partial end-stage OA
Interventions	r-UKR (robot-assisted unicompartimental KA)
Comparator	UKR (conventional unicompartimental KA)
Analytic Method	Deterministic
Modelling	Decision-tree + Markov model
Effectiveness	Treatment effect was modelled directly in terms of revision rates Annual probability of revision for a conventional UKR = 1.5% (weighted mean of failure rates from 15 studies) Probability of revision using robots was set at 0.55% annually for the first 2 years (based on a conference abstract about a (observational?) study of 2-year failure rates in 710 robot-assisted implants, robot type not reported). After the first 2 years, rates were similar to the conventional UKR Assumed only 1 revision over the time horizon Utilities: Primary UKR 0.75; Revision to TKR 0.565; Disutility for revision to TKR 0.102
Country	USA
Perspective	Payer perspective
Time Horizon	Lifetime
Discount Rate (Costs & Outcomes)	3%
Cycle length	1-year
Reported Outcomes	QALYs, costs
Resource Use and Costs	Cost based on MAKO's vendors, amortized over 100 cases per year, over 5-year lifespan of the equipment; 2012 USD$
Uncertainty/ Sensitivity analysis	1-way and 2-way sensitivity analysis including different volumes, revision rates for the robot, robot costs and lifetime, utilities after primary and revision surgery and patient age

NMA= Network meta-analysis; QALYs=Quality-adjusted life years; NR=not reported; INMB= incremental net monetary benefits; MCER=marginal cost-effectiveness ratio; ICER=incremental cost-effectiveness ratio; NIHR= National Institute for Health Research