Quality-Based Procedures Clinical Handbook for Primary Hip and Knee Replacement

Health Quality Ontario & Ministry of Health and Long-Term Care

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards (EDS) Branch at Health Quality Ontario (HQO) are impartial. There are no competing interests or conflicts of interest to declare.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. Health Quality Ontario works with clinical experts, scientific collaborators, and field evaluation partners to develop and publish research that evaluates the effectiveness and cost-effectiveness of health technologies and services in Ontario.

Based on the research conducted by Health Quality Ontario and its partners, the Ontario Health Technology Advisory Committee (OHTAC)—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy makers.

Rapid reviews, evidence-based analyses and their corresponding OHTAC recommendations, and other associated reports are published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About the Quality-Based Procedures Clinical Handbooks

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Disclaimer

The content in this document has been developed through collaborative efforts between the Ministry of Health and Long-Term Care ("Ministry"), the Evidence Development and Standards (EDS) Branch at Health Quality Ontario (HQO), and Expert Advisory Panel on Episode of Care for Primary Hip and Knee Replacement ("Expert Panel"). The template for the Quality-Based Procedures Clinical Handbook and all content in the "Purpose" and "Introduction to Quality-Based Procedures" sections were provided in standard form by the Ministry. All other content was developed by HQO with input from the Expert Panel. As it is based in part on rapid reviews and expert opinion, this handbook may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its reports. In addition, it is possible that other relevant scientific findings may have been reported since completion of the handbook and/or rapid reviews. This report is current to the date of the literature search specified in the Research Methods section of each rapid review. This handbook may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all HQO's Quality-Based Procedures Clinical Handbooks: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

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List of Abbreviations

AGREE II	Appraisal of Guidelines for Research & Evaluation II
ALC	Alternate Level of Care
ASA	American Society of Anesthesiologists
BOA	British Orthopaedic Association
CCI	Canadian Classification of Interventions
CIHI	Canadian Institute for Health Information
COPD	Chronic obstructive pulmonary disease
DAD	Discharge Abstract Database
ED	Emergency department
HBAM	Health-Based Allocation Model
HIG	Health-Based Allocation Model Inpatient Grouper
HQO	Health Quality Ontario
HSFR	Health System Funding Reform
ICD	International Classification of Diseases
LHIN	Local Health Integration Network
LOS	Length of stay
MRDx	Most responsible diagnosis
NACRS	National Ambulatory Care Reporting System
NSW	New South Wales
OCCI	Ontario Case Costing Initiative
OHTAC	Ontario Health Technology Advisory Committee
PBF	Patient-Based Funding
PCP	Primary care provider
QBP	Quality-Based Procedure
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Preface

The content in this document has been developed through collaborative efforts between the Ministry of Health and Long-Term Care (the "Ministry"), Health Quality Ontario (HQO), and the HQO Expert Advisory Panel on Episode of Care for Primary Hip and Knee Replacement (the "Expert Panel").

The template for the Quality-Based Procedures Clinical Handbook and all content in Section 1 ("Purpose") and Section 2 ("Introduction to Quality-Based Procedures") were provided in standard form by the Ministry. All other content was developed by HQO with input from the Expert Panel.

To consider the content of this document in the appropriate context, it is important to take note of the specific deliverables that the Ministry tasked HQO with developing for this Clinical Handbook. The following includes excerpts from the HQO–Ministry Accountability Agreement for fiscal year 2013/14:

> *To guide HQO's support to the funding reform, HQO will:*
>
> - *Conduct analyses/consultation in the following priority areas in support of funding strategy implementation for the 2014/15 fiscal year:*
>   - *Pneumonia*
>   - *Primary hip and knee replacement*
>
> - *Include in their analyses/consultation noted in the previous clause, consultations with clinicians and scientists who have knowledge and expertise in the identified priority areas, either by convening a reference group or engaging an existing resource of clinicians/scientists*.
>
> - *Work with the reference group to:*
>
>   *a) define the population/patient cohorts for analysis,*
>
>   *b) define the appropriate episode of care for analysis in each cohort, and*
>
>   *c) seek consensus on a set of evidence-based clinical pathways and standards of care for each episode of care.*

The Ministry also asked HQO to make recommendations on performance indicators aligned with the recommended episodes of care to inform the Ministry's Quality-Based Procedure (QBP) Integrated Scorecard and to provide guidance on the real-world implementation of the recommended practices contained in the Clinical Handbook, with a focus on implications for multidisciplinary teams, service capacity planning considerations, and new data collection requirements.

HQO was asked to produce the deliverables described above using the Clinical Handbook template structure provided by the Ministry.

Key Principles

An initial set of key principles or "ground rules" has been established in discussions between HQO, the Expert Panels, and the Ministry to guide future episode of care work:

- **HQO's work does not involve costing or pricing.** All costing and pricing work related to the QBP funding methodology will be completed by the Ministry using a standardized approach, informed by the content produced by HQO. This principle also extended to the deliberations of the Expert Panels, where discussions were steered away from considering the dollar cost of particular interventions or models of care and instead focused on considerations around quality and the impact of patient characteristics on variation in care pathways and resource utilization.
- **Recommended practices, supporting evidence, and policy applications will be reviewed and updated at least every 2 years.** The limited 5-month time frame provided for the completion of this work meant that many of the recommended practices in this document could not be assessed with the full rigour and depth of HQO's established evidence-based analysis process. Recognizing this limitation, HQO reserves the right to revisit the recommended practices and supporting evidence at a later date by conducting a full evidence-based analysis or to update this document with relevant newly published research. In cases where the episode of care models are updated, any policy applications informed by the models should also be similarly updated.
- **Recommended practices should reflect the best patient care possible.** HQO and the Expert Panels were instructed to focus on defining best practice for an *ideal* episode of care, regardless of cost implications or potential barriers to access. Hence, the resulting cost implications of the recommended episodes of care are not known. However, the Expert Panels have discussed a number of barriers that will challenge implementation of their recommendations across the province. These include gaps in measurement capabilities for tracking many of the recommended practices, shortages in health human resources, and limitations in community-based care capacity across many parts of the province.
- Some of these barriers and challenges are briefly addressed in the "Implementation Considerations" section of this Handbook. However, the Expert Panels noted that with the limited time they were provided to address these issues, the considerations outlined here should be viewed only as an initial starting point towards a comprehensive analysis of these challenges.

Finally, HQO and the Expert Panel recognize that, given the limitations of their mandate, much of the ultimate impact of this content will depend on subsequent work by the Ministry to incorporate the analysis and advice contained in this document into the Quality-Based Procedures policy framework and funding methodology. This will be complex work, and it will be imperative to ensure that any new funding mechanisms deployed are aligned with the recommendations of the Expert Panel.

Nevertheless, the Expert Panel believes that, regardless of the outcome of efforts to translate this content into hospital funding methodology, the recommended practices in this document can also provide the basis for setting broader provincial standards of care for primary hip and knee replacement patients. These standards could be linked not only to funding mechanisms, but to other health system change levers such as guidelines and care pathways, performance measurement and reporting, program planning, and quality improvement activities.

Purpose

Provided by the Ministry of Health and Long-Term Care

This Clinical Handbook has been created to serve as a compendium of the evidence-based rationale and clinical consensus driving the development of the policy framework and implementation approach for primary hip and knee replacement patients seen in hospitals.

This document has been prepared for informational purposes only. This document does not mandate health care providers to provide services in accordance with the recommendations included herein. The recommendations included in this document are not intended to take the place of the professional skill and judgment of health care providers.

Introduction to Quality-Based Procedures

Provided by the Ministry of Health and Long-Term Care

Quality-Based Procedures (QBPs) are an integral part of Ontario's Health System Funding Reform (HSFR) and a key component of Patient-Based Funding (PBF). This reform plays a key role in advancing the government's quality agenda and its **Action Plan for Health Care.** HSFR has been identified as an important mechanism to strengthen the link between the delivery of high quality care and fiscal sustainability.

Ontario's health care system has been living under global economic uncertainty for a considerable time. Simultaneously, the pace of growth in health care spending has been on a collision course with the provincial government's deficit recovery plan.

In response to these fiscal challenges and to strengthen the commitment towards the delivery of high quality care, the ***Excellent Care for All Act*** (*ECFAA*) received royal assent in June 2010. ECFAA is a key component of a broad strategy that improves the quality and value of the patient experience by providing them with the right evidence-informed health care at the right time and in the right place. ECFAA positions Ontario to implement reforms and develop the levers needed to mobilize the delivery of high quality, patient-centred care.

Ontario's **Action Plan for Health Care** advances the principles of *ECFAA*, reflecting quality as the primary driver to system solutions, value, and sustainability.

What Are We Moving Towards?

Prior to the introduction of HSFR, a significant proportion of hospital funding was allocated through a global funding approach, with specific funding for some select provincial programs and wait times services. However, a global funding approach reduces incentives for health service providers to adopt best practices that result in better patient outcomes in a cost-effective manner.

To support the paradigm shift from a culture of cost containment to that of quality improvement, the Ontario government is committed to moving towards a patient-centred, evidence-informed funding model that reflects local population needs and contributes to optimal patient outcomes (Figure 1).

PBF models have been implemented internationally since 1983. Ontario is one of the last leading jurisdictions to move down this path. This puts the province in a unique position to learn from international best practices and the lessons others learned during implementation, thus creating a funding model that is best suited for Ontario.

PBF supports system capacity planning and quality improvement through directly linking funding to patient outcomes. PBF provides an incentive to health care providers to become more efficient and effective in their patient management by accepting and adopting best practices that ensure Ontarians get the right care at the right time and in the right place.

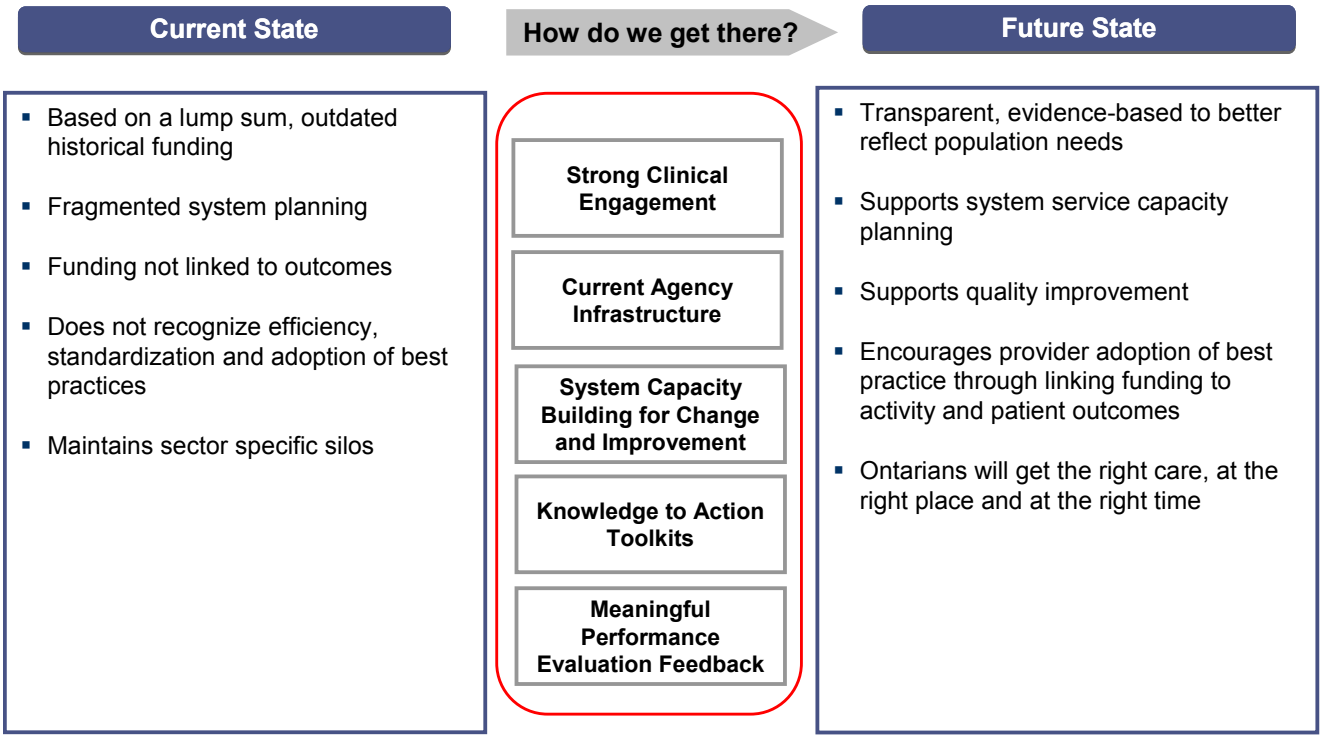

Figure 1. Current and Future States of Health System Funding

How Will We Get There?

The Ministry of Health and Long-Term Care has adopted a 3-year implementation strategy to phase in a PBF model and will make modest funding shifts starting in fiscal year 2012/2013. A 3-year outlook has been provided to support planning for upcoming funding policy changes.

The Ministry has released a set of tools and guiding documents to further support the field in adopting the funding model changes. For example, a QBP interim list has been published for stakeholder consultation and to promote transparency and sector readiness. The list is intended to encourage providers across the continuum to analyze their service provision and infrastructure in order to improve clinical processes and, where necessary, build local capacity.

The successful transition from the current, provider-centred funding model towards a patient-centred model will be catalyzed by a number of key enablers and field supports. These enablers translate to actual principles that guide the development of the funding reform implementation strategy related to QBPs. These principles further translate into operational goals and tactical implementation (Figure 2).

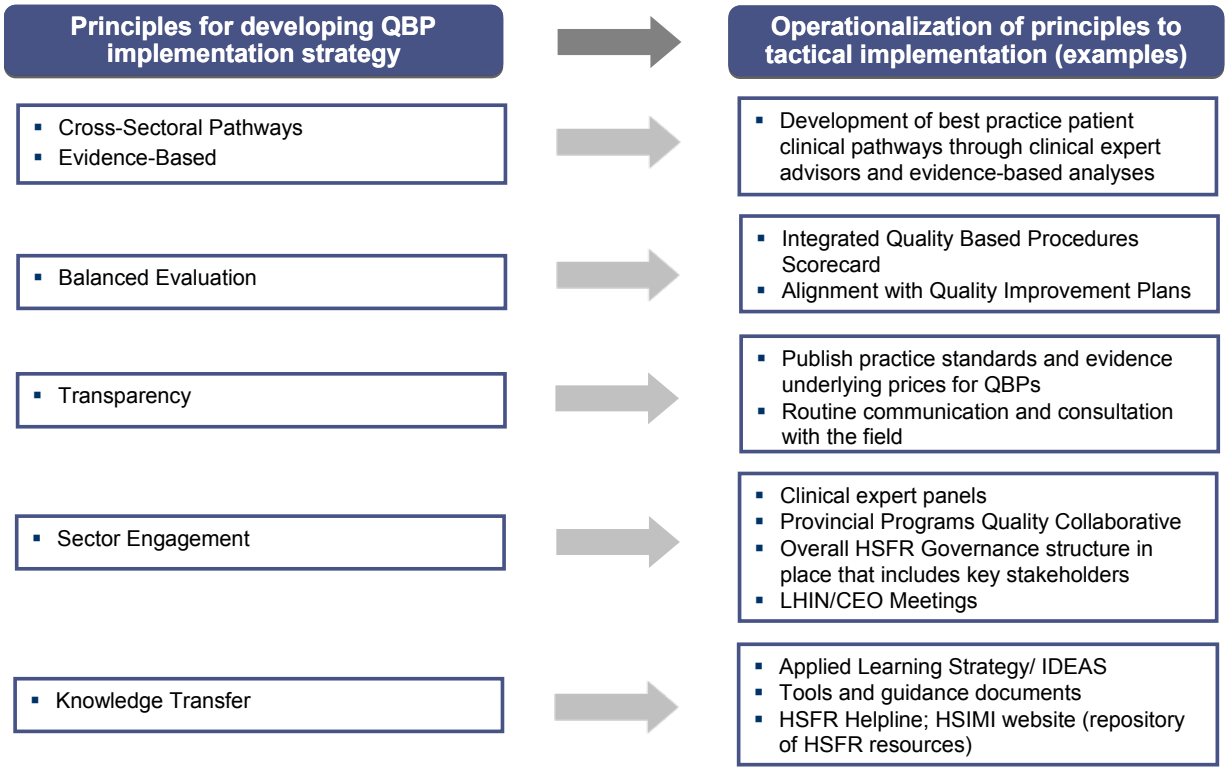

Figure 2. Principles Guiding Implementation of Quality-Based Procedures

Abbreviations: HSIMI, Health System Information Management and Investment; IDEAS, Improving the Delivery of Excellence Across Sectors; LHIN, Local Health Integration Network.

What Are Quality-Based Procedures?

QBPs involve clusters of patients with clinically related diagnoses or treatments. Primary hip and knee replacement was chosen as a QBP using an evidence- and quality-based selection framework that identifies opportunities for process improvements, clinical redesign, improved patient outcomes, enhanced patient experience, and potential cost savings.

The evidence-based framework used data from the Discharge Abstract Database (DAD) adapted by the Ministry of Health and Long-Term Care for its Health-Based Allocation Model (HBAM) repository. The HBAM Inpatient Grouper (HIG) groups inpatients based on their diagnosis or their treatment for the majority of their inpatient stay. Day surgery cases are grouped in the National Ambulatory Care Referral System (NACRS) by the principal procedure they received. Additional data were used from the Ontario Case Costing Initiative (OCCI). Evidence in publications from Canada and other jurisdictions and World Health Organization reports was also used to assist with the patient clusters and the assessment of potential opportunities.

The evidence-based framework assessed patients using 4 perspectives, as presented in Figure 3. This evidence-based framework has identified QBPs that have the potential to both improve quality outcomes and reduce costs.

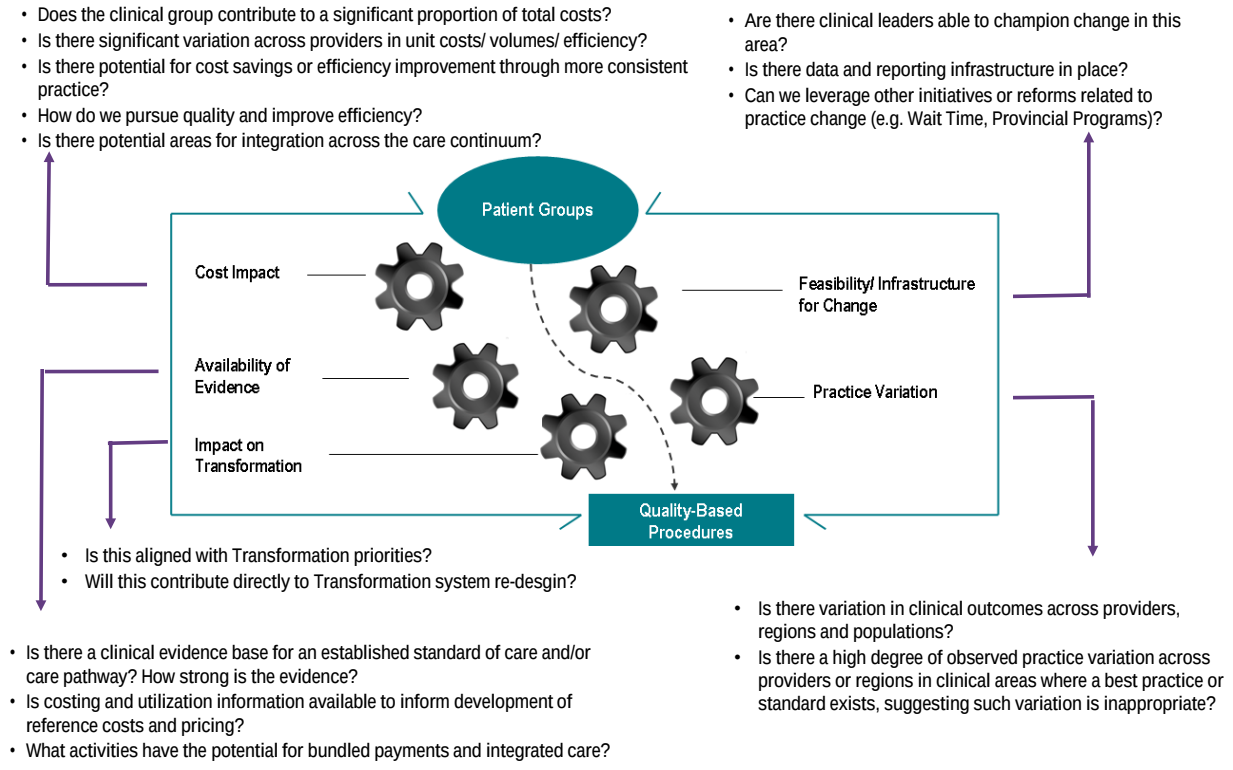

Figure 3. Evidence-Based Framework

Practice Variation

The DAD stores every Canadian patient discharge, coded and abstracted, for the past 50 years. This information is used to identify patient transition through the acute care sector, including discharge locations, expected lengths of stay (LOS) and readmissions for each and every patient, based on their diagnosis and treatment, age, sex, comorbidities and complexities, and other condition-specific data. A demonstrated large practice or outcome variance may represent a significant opportunity to improve patient outcomes by reducing this practice variation and focusing on evidence-informed practice. A large number of "Beyond Expected Days" for LOS and a large standard deviation for LOS and costs are flags to such variation. Ontario has detailed case-costing data for all patients discharged from a case-costing hospital from as far back as 1991, as well as daily utilization and cost data by department, by day, and by admission.

Availability of Evidence

A significant amount of Canadian and international research has been undertaken to develop and guide clinical practice. Using these recommendations and working with the clinical experts, best practice guidelines and clinical pathways can be developed for these QBPs, and appropriate evidence-informed indicators can be established to measure performance.

Feasibility/Infrastructure for Change

Clinical leaders play an integral role in this process. Their knowledge of the patients and the care provided or required represents an invaluable component of assessing where improvements can and should be made. Many groups of clinicians have already provided evidence for rationale-for-care pathways and evidence-informed practice.

Cost Impact

The selected QBP should have no fewer than 1,000 cases per year in Ontario and represent at least 1% of the provincial direct cost budget. While cases that fall below these thresholds may, in fact, represent improvement opportunity, the resource requirements to implement a QBP may inhibit the effectiveness for such a small patient cluster, even if there are some cost efficiencies to be found. Clinicians may still work on implementing best practices for these patient subgroups, especially if they align with the change in similar groups. However, at this time, there will be no funding implications. The introduction of evidence into agreed-upon practice for a set of patient clusters that demonstrate opportunity as identified by the framework can directly link quality with funding.

QBP Evidence-Based Framework for Primary Hip and Knee Replacement

(Reproduced from MOHLTC June 2012 Quality-Based Procedures Clinical Handbook for Primary Unilateral Hip Replacement)

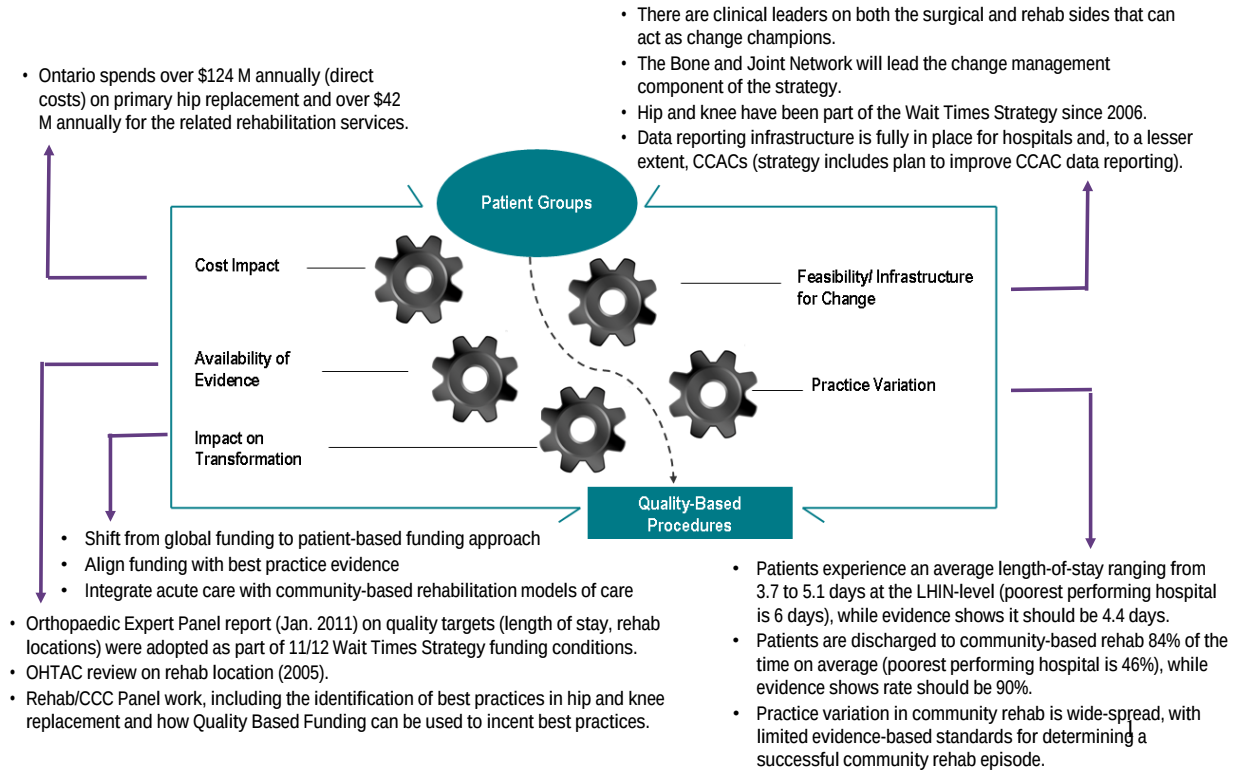

Figure 4. Quality-Based Procedures Evidence-Based Framework for Primary Hip Replacement

How Will Quality-Based Procedures Encourage Innovation in Health Care Delivery?

Implementing evidence-informed pricing for the targeted QBPs will encourage health care providers to adopt best practices in their care delivery models and maximize their efficiency and effectiveness. Moreover, best practices that are defined by clinical consensus will be used to understand required resource utilization for the QBPs and further assist in developing evidence-informed pricing.

Implementation of a "price × volume" strategy for targeted clinical areas will motivate providers to:

- adopt best practice standards
- re-engineer their clinical processes to improve patient outcomes
- develop innovative care delivery models to enhance the experience of patients

Clinical process improvement may include better discharge planning, eliminating duplicate or unnecessary investigations, and paying greater attention to the prevention of adverse events, that is, postoperative complications. These practice changes, together with adoption of evidence-informed practices, will improve the overall patient experience and clinical outcomes and help create a sustainable model for health care delivery.

Methods

Overview of the Health Quality Ontario Episode of Care Analysis Approach

To produce this work, Health Quality Ontario (HQO) has developed a novel methodology known as an *episode of care analysis* that draws conceptually and methodologically from several of HQO's core areas of expertise:

- **Health technology assessment**: Recommended practices incorporate components of HQO's evidence-based analysis methodology and draw from the recommendations of the Ontario Health Technology Advisory Committee (OHTAC).
- **Case mix grouping and funding methodology:** Cohort and patient group definitions use clinical input to adapt and refine case mix methodologies from the Canadian Institute for Health Information (CIHI) and the Ontario HBAM.
- **Clinical practice guidelines and pathways:** Recommended practices synthesize guidance from credible national and international guideline bodies, with attention to the strength of evidence supporting each piece of guidance.
- **Analysis of empirical data:** Expert Panel recommendations are supported by descriptive and multivariate analysis of Ontario administrative data (e.g., DAD and NACRS) and data from disease-based clinical data sets (e.g., the Ontario Stroke Audit [OSA] and Enhanced Feedback For Effective Cardiac Treatment [EFFECT] databases). HQO works with researchers and Ministry of Health and Long-Term Care ("Ministry") analytic staff to develop analyses for the Expert Panel's review.
- **Clinical engagement**: All aspects of this work were guided and informed by leading clinicians, scientists, and administrators with a wealth of knowledge and expertise in the clinical area of focus.
- **Performance indicators**: HQO has been asked to leverage its expertise in performance indicators and public reporting to support the development of measurement frameworks to manage and track actual performance against the recommended practices in the episodes of care.

The development of the episode of care analysis involves the following key steps:

- **Defining the cohort and patient stratification approach**
- **Defining the scope of the episode of care**
- **Developing the episode of care model**
- **Identifying recommended practices, including the rapid review process**
- **Supporting the development of performance indicators to measure the episode of care**

The following sections describe each of these steps in further detail.

Defining the Cohort and Patient Stratification Approach

At the outset of this project, the Ministry provided HQO with a broad description of each assigned clinical population (e.g., stroke), and asked HQO to work with the Expert Panels to define inclusion and exclusion criteria for the cohort they would examine using data elements from routinely reported provincial administrative databases. It was also understood that each of these populations might encompass multiple distinct subpopulations (referred to as "patient groups") with significantly different clinical characteristics. For example, the congestive heart failure (CHF) population includes subpopulations with heart failure, myocarditis, and cardiomyopathies. These patient groups each have very different levels of severity, different treatment pathways, and different distributions of expected resource utilization. Consequently, these groups may need to be reimbursed differently from a funding policy perspective.

Conceptually, the process employed here for defining cohorts and patient groups shares many similarities with methods used around the world for the development of case mix methodologies, such as Diagnosis-Related Groups (DRGs) or the Canadian Institute for Health Information's Case Mix Groups. Case mix methodologies have been used since the late 1970s to classify patients into groups that are similar in terms of both clinical characteristics and resource utilization for the purposes of payment, budgeting, and performance measurement. (1) Typically, these groups are developed using statistical methods such as classification and regression tree analysis to cluster patients with similar costs based on common diagnoses, procedures, age, and other variables. After the initial patient groups have been established based on statistical criteria, clinicians are often engaged to ensure that the groups are clinically meaningful. Patient groups are merged, split, and otherwise reconfigured until the grouping algorithm reaches a satisfactory compromise between cost prediction, clinical relevance, and usability. Most modern case mix methodologies and payment systems also include a final layer of patient complexity factors that modify the resource weight (or price) assigned to each group upward or downward. These can include comorbidities, use of selected interventions, long- or short-stay status, and social factors.

In contrast with these established methods for developing case mix systems, the patient classification approach that the Ministry asked HQO and the Expert Panels to undertake is unusual in that it *begins* with the input of clinicians rather than with statistical analysis of resource utilization. The Expert Panels were explicitly instructed not to focus on cost considerations but instead to rely on their clinical knowledge of those patient characteristics that are commonly associated with differences in indicated treatments and expected resource utilization. Expert Panel discussions were also informed by summaries of relevant literature and descriptive tables containing Ontario administrative data.

Based on this information, the Expert Panels recommended a set of inclusion and exclusion criteria to define each disease cohort. Starting with identifying the ICD-10-CA* diagnosis codes for the population, the Expert Panels then excluded diagnoses with significantly different treatment protocols from that required for the general population, including pediatric cases and patients with very rare disorders. Next, the Expert Panels recommended definitions for major patient groups within the cohort. Finally, the Expert Panels identified patient characteristics that they believe would contribute to additional resource utilization for patients within each group. This process generated a list of factors ranging from commonly occurring comorbidities to social characteristics such as housing status.

*International Classification of Diseases, 10th Revision (Canadian Edition).

In completing the process described above, the Expert Panel encountered some noteworthy challenges:

- **Absence of clinical data elements capturing important patient complexity factors.** The Expert Panels quickly discovered that a number of important patient-based factors related to the severity of patients' conditions or their expected utilization are not routinely collected in Ontario hospital administrative data. These include both key clinical measures (such as FEV_1 / FVC for chronic obstructive pulmonary disease [COPD] patients and AlphaFIM®[†] scores for stroke patients) as well as important social characteristics (such as caregiver status).[‡] For stroke and CHF, some of these key clinical variables have been collected in the past through the OSA and EFFECT datasets, respectively. However, these datasets were limited to a group of participating hospitals and at this time are not funded for future data collection.
- **Limited focus on a single disease or procedure grouping within a broader case mix system.** While the Expert Panels were asked to recommend inclusion/exclusion criteria only for the populations tasked to them, the patient populations assigned to HQO are a small subset of the many patient groups under consideration for Quality-Based Procedures. This introduced some additional complications when defining population cohorts; after the Expert Panels had recommended their initial patient cohort definitions (based largely on diagnosis), the Ministry informed the Expert Panels that there were a number of other patient groups planned for future QB) funding efforts that overlapped with the cohort definitions.

  For example, while the vast majority of patients discharged from hospital with a most responsible diagnosis (MRDx) of COPD receive largely ward-based medical care, a small group of COPD-diagnosed patients receive much more cost-intensive interventions such as lung transplants or resections. Based on their significantly different resource utilization, the Ministry's HBAM grouping algorithm assigns these patients to a different HIG group from the general COPD population. Given this methodological challenge, the Ministry requested that the initial cohorts defined by the Expert Panels be modified to exclude patients that receive selected major interventions. It is expected that these patients may be assigned to other QBP patient groups in the future. This document presents both the initial cohort definition defined by the Expert Panel and the modified definition recommended by the Ministry.

In short, the final cohorts and patient groups described here should be viewed as a compromise solution based on currently available data sources and the parameters of the Ministry's HBAM grouping methodology.

[†]The Functional Independence Measure (FIM) is a composite measure consisting of 18 items assessing 6 areas of function. These fall into 2 basic domains; physical (13 items) and cognitive (5 items). Each item is scored on a 7-point Likert scale indicative of the amount of assistance required to perform each item (1 = total assistance, 7 = total independence). A simple summed score of 18–126 is obtained where 18 represents complete dependence / total assistance and 126 represents complete independence.

[‡]For a comprehensive discussion of important data elements for capturing various patient risk factors, see Iezzoni LI, editor. Range of risk factors. In Iezzoni LI (Ed.) Risk adjustment for measuring health care outcomes, 4th ed. Chicago: Health Administration Press; 2012. p. 29-76.

Defining the Scope of the Episode of Care

HQO's episode of care analysis draws on conceptual theory from the emerging worldwide use of episode-based approaches for performance measurement and payment. Averill et al. (1), Hussey et al. (2) and Rosen and Borzecki (3) describe the key parameters required for defining an appropriate episode of care:

- **Index event:** The event or time point triggering the start of the episode. Examples of index events include admission for a particular intervention, presentation at the emergency department (ED) or the diagnosis of a particular condition.
- **Endpoint:** The event or time point triggering the end of the episode. Examples of endpoints include death, 30 days following hospital discharge, or a "clean period" with no relevant health care service utilization for a defined period.
- **Scope of services included:** Although an "ideal" episode of care might capture all health and social care interventions received by the patient from index event to endpoint, in reality not all these services may be relevant to the objectives of the analysis. Hence, the episode may exclude some types of services such as prescription drugs or services tied to other unrelated conditions.

Ideally, the parameters of an episode of care are defined based on the nature of the disease or health problem studied and the intended applications of the episode (e.g., performance measurement, planning, or payment). For HQO's initial work here, many of these key parameters were set in advance by the Ministry based on the government's QBP policy parameters. For example, in 2013/2014 the QBPs will focus on reimbursing acute care, and do not include payments for physicians or other non-hospital providers. These policy parameters resulted in there being limited flexibility to examine non-hospital elements such as community-based care or readmissions.

Largely restricted to a focus on hospital care, the Chairs of the Expert Panel recommended that the episodes of care for primary hip and knee replacement begin with a patient's presentation to the ED (rather than limit the analysis to the inpatient episode) in order to provide scope to examine criteria for admission. Similarly, the Expert Panels ultimately also included some elements of postdischarge care in the scope of the episode in relation to discharge planning in the hospital and the transition to community services.

Developing the Episode of Care Pathway Model

HQO has developed a model that brings together the key components of the episode of care analysis through an integrated schematic. The model is structured around the parameters defined for the episode of care, including boundaries set by the index event and endpoints, segmentation (or stratification) of patients into the defined patient groups, and relevant services included in the episode. The model describes the pathway of each patient case included in the defined cohort, from initial presentation through segmentation into one of the defined patient groups based on their characteristics, and finally through the subsequent components of care that they receive before reaching discharge or endpoint otherwise defined.

Although the model bears some resemblance to a clinical pathway, it is not intended to be used as a traditional operational pathway for implementation in a particular care setting. Rather, the model presents the critical decision points and phases of treatment within the episode of care, referred to here as *clinical assessment nodes* and *care modules*, respectively. Clinical assessment nodes (CANs) provide patient-specific criteria for whether a particular case proceeds down one branch of the pathway or another. Once patients move down a particular branch, they then receive a set of recommended practices that are clustered together as a care module. Care modules represent the major phases of care that patients receive during a hospital episode, such as treatment in the ED, care on the ward, and discharge planning. The process for identifying the recommended practices within each CAN and care module is described in the next section.

Drawing from the concepts of decision analytic modelling, the episode of care model includes crude counts (N) and proportions (Pr) of patients proceeding down each branch of the pathway model. For the Primary Hip and Knee Replacement Clinical Handbook, these counts were determined based on utilization data from administrative databases including the DAD, NACRS, and for some populations, specialized clinical registry data. These counts are based on current Ontario practice, and are not intended to represent normative or ideal practice. For some clinical populations, evidence-informed targets have been set at certain CANs for the proportions of patients that should ideally proceed down each branch. For example, a provincial target has been set for 90% of primary hip and knee replacement patients to be discharged home (versus discharged to an inpatient rehabilitation setting) from acute care, based on a 2005 OHTAC recommendation. Where relevant, these targets have been included in the episode model.

Figure 5 provides an example of a care module and CAN:

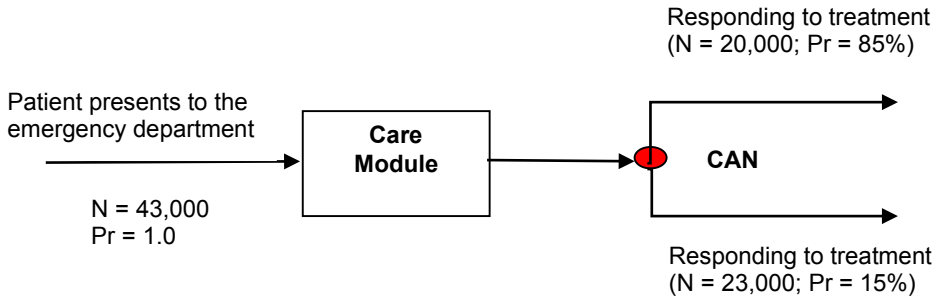

Figure 5. Example Episode of Care Model
Abbreviations: CAN, clinical assessment node; N, crude counts; Pr, proportions.

Identifying Recommended Practices

Considering Evidence Sources

A number of different evidence sources were considered and presented to the Expert Panel to develop the episode of care model and populate individual modules with best practice recommendations. Preference was given to OHTAC recommendations. Where OHTAC recommendations did not exist, additional evidence sources included guidance from guidelines and other evidence-based organizations, HQO rapid reviews, empirical analysis of Ontario data, and where necessary and appropriate, expert consensus.

OHTAC Recommendations

OHTAC recommendations are considered the gold standard of evidence for several reasons:

- **Consistency:** While many guidance bodies issue disease-specific recommendations, OHTAC provides a common evidence framework across all the clinical areas analyzed in all disease areas.
- **Economic modelling:** OHTAC recommendations are often supported by economic modelling to determine the cost-effectiveness of an intervention, whereas many guidance bodies assess only effectiveness.
- **Decision-Making Framework:** OHTAC recommendations are guided by a decision determinants framework that considers the clinical benefit offered by a health intervention, in addition to value for money; societal and ethical considerations; and economic and organizational feasibility.
- **Contextualization:** In contrast with recommendations and analyses from international bodies, OHTAC recommendations are developed through the contextualization of evidence for Ontario. This ensures that the evidence is relevant to the Ontario health system.

Clinical Guidelines

Published Canadian and international guidelines that take into account the entire primary hip and knee arthroplasty pathway were searched for with the help of HQO medical librarians. In addition, the Expert Panel was further consulted to ensure all relevant guidelines were identified.

The methodological rigour and transparency of clinical practice guidelines was determined using the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument. (4) AGREE II is made up of 6 domains that capture guideline quality. These domains, which influence potential benefit, include scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. (4) The AGREE domain scores provide information about the relative quality of the guideline, with higher scores reflecting use of appropriate methodologies and rigorous strategies in the development process to a greater extent. Guidelines were selected for inclusion based on evaluation of the individual AGREE scores, with an emphasis on the rigour of development domain score. This domain reflects the strength of the methods used to assess the quality of evidence supporting the guideline recommendations. The final selection of guidelines included a minimum of 1 contextually relevant guideline (i.e., a Canadian guideline) and 3 to 4 additional best quality guidelines, when available.

The contextually relevant or Canadian guideline served as the baseline for and was directly compared to the other included guidelines. The quality of the evidence supporting each recommendation, as assessed and reported by the published guidelines, was identified. Inconsistencies and gaps across recommendations were noted for potential further evaluation.

Rapid Reviews

Where there was inconsistency across guidelines, disagreement among expert panel members, or uncertainty around the evidence for a best practice, an HQO evidence review was considered. Recognizing that a full evidence-based analysis would be impractical for all topics, a rapid evidence review process was used to identify the best evidence within the compressed time frame of developing the entire episode of care pathway (see Appendix). Where a rapid review was deemed insufficient or inappropriate to answer the evidence question, a full evidence-based analysis was considered.

Analysis of Administrative and Clinical Data

In addition to evidence reviews of the published literature, the Expert Panel also examined the results of descriptive and multivariate analysis using Ontario administrative and clinical datasets. Multivariate analyses were developed modelling patient characteristics such as age, diagnoses, and procedures for their association with outcomes of interest such as length of stay, resource utilization, and mortality. Dependent (outcome) and independent variables for analysis were identified by Expert Panel members based on their clinical experience and their review of summaries of the literature evaluating the association between patient characteristics and a range of outcomes. The Expert Panel also provided advice on the analytical methods used, including datasets included and the most appropriate functional forms of the variables modelled.

Other analyses reviewed based on Ontario administrative data included studies of current utilization patterns such as average hospital LOS and studies of regional variation across Ontario in admission practices and hospital discharge settings.

Expert Consensus

The Expert Panel contextualized the best evidence for the Ontario health care system to arrive at the best practice recommendations (see Recommended Practices section). Where the available evidence was limited or nonexistent, recommendations were made based on consensus agreement by the Expert Panel.

Description of Primary Hip and Knee Replacement

Primary hip and knee replacement—also known as replacement arthroplasty—is a surgical procedure involving the replacement of an arthritic or dysfunctional joint surface with an orthopedic prosthesis. The majority of patients undergoing joint replacement surgery are treated for osteoarthritis, with a smaller proportion (approximately 4%) treated for rheumatoid arthritis. (5) Joint replacement surgery is typically indicated in cases of severe joint pain or dysfunction that conservative therapies such as anti-inflammatory medications, activity modification, and weight loss do not alleviate. (6-8) Under these indications, a large body of research has found that joint replacement is a highly effective intervention that can provide significant improvements in function, pain relief, and health-related quality of life. (5;9-16) Health technology assessments developed in a number of countries have found joint replacement surgery to be very cost-effective (5;11-13) and even cost-saving in certain patient subgroups when compared with the costs of long-term non-surgical management. (13)

Optimal joint replacement care involves a multidisciplinary team and an evidence-based care pathway extending from referral for an orthopedic consultation through surgery to rehabilitation and convalescence. (17;18) Appropriate perioperative management includes the use of pre-operative diagnostics, comorbidity screening, blood management, antibiotic prophylaxis, and postoperative mobilization. (17;18) Following discharge from acute care, joint replacement patients typically receive a program of rehabilitation provided in either a dedicated inpatient setting or through a variety of outpatient modalities including home- and clinic-based settings. (19)

The number of joint replacements performed in Canada increased by 87% from 1994/1995 to 2004/2005 (20) and by 13% between 2006–2007 and 2010–2011 to an annual total of 93,446 hip and knee replacement hospitalizations across Canada. (21) This growth has been driven in large part by federal and provincial efforts to reduce wait times, most notably the First Ministers' 2005 consensus agreement on a national target of 90% of patients receiving surgery within 182 days following the decision to treat. (19) In Ontario, the provincial government's Wait Time Strategy has brought even more dramatic growth in surgical volumes than in other provinces, with the number of joint replacement procedures performed rising by 51% between August–September 2005 and February 2009 (22) to steady state volumes of 11,620 elective primary hip replacements, 21,466 elective primary knee replacements, and 508 elective simultaneous bilateral joint replacements in the 2011/2012 fiscal year. (23) The average age of these patients was 67 years; 54.6% of hip replacement patients and 61.7% of knee replacement patients were female. (23) Consistent with international studies, (5) osteoarthritis was recorded as the MRDx in over 90% of hip replacements and 95% of knee replacements. (23)

Joint replacements have a considerable impact on provincial health care expenditures. Not only are they among the most common reasons for hospitalization, but they also come with a significant price tag: their average acute care costs are $10,125 and $9,295 for hip and knee replacement, respectively, with total episode of care costs of $15,863 and $14,192 when the costs of physician services and post-acute care within 30 days of hospital discharge are included. (24) Overall, primary joint replacements account for approximately $500 million in annual Ontario health care spending. (23;24)

The large volume and considerable cost impact of joint replacement surgery has made it the focus of significant province-wide changes in practice, organization, and access over the past decade. The aforementioned Wait Times Strategy allocated case-based funding to hospitals to expand their surgical volumes, decreasing average wait times by 56.4% for hip replacement and 58.2% for knee replacement between August–September 2005 and February 2009 and bringing Ontario—alone among the

provinces—within the 90% / 182-day benchmark for hip replacement. (22;25) Recent Wait Times Information System data shows that provincial performance has slipped slightly since this high point: current 90th percentile wait times exceed the 182-day target, running at 188 days for hip replacement and 214 days for knee replacement (26).

Ontario government investments have recently shifted from improving access to joint replacement to focusing on appropriateness. As of 2009, there has been a province-wide policy-driven push away from inpatient rehabilitation following joint replacement towards less resource-intensive outpatient rehabilitation. This shift in practice has been supported by high quality Ontario evidence showing that home-based rehabilitation is equally effective and considerably more cost-effective compared with inpatient rehabilitation. (27) This evidence has led to a 2005 Ontario Health Technology Advisory Committee recommendation (28;29) and the Ontario Orthopaedic Expert Panel's establishment of a provincial target for 90% of joint replacement patients to be discharged home from acute care (30). These evidence-based standards of care were implemented through clinical leadership and quarterly hospital-level performance reporting as well as feedback through the Orthopaedic Quality Scorecard produced by Access to Care at Cancer Care Ontario. (31) As a result, the changes in practice over a relatively short period of time have been dramatic: from baseline performance in 2009/2010 of 8 of the 14 Local Health Integration Networks (LHINs) performing below the 90% discharge home target to only one LHIN still below target by Q3 2012/2013. Over the same period, the provincial rate of patients discharged home following joint replacement increased from 74.8% to 91.8%, (32;33) resulting in efficiency savings of approximately $19 million.§ Even more importantly, this practice shift has freed up inpatient rehabilitation beds for use by more complex stroke and hip fracture patients that require the additional level of care provided in these settings. This has helped reduce Alternate Level of Care (ALC) pressures on acute care beds by these stroke and hip fracture patient populations, thus improving their functional outcomes (30).

Recent efficiency improvements have been driven by the same combination of provincial clinical leadership and performance reporting. Following the Orthopaedic Expert Panel's establishment of a 4.4-day benchmark average acute LOS (31), provincial average acute LOS has dropped from 4.8 days in 2009/10 to 4.0 days in Q3 2012/2013 (32;33).

Most recently, primary hip and knee replacement has been targeted for funding reform as part of the 2012/2013 roll-out of the government's QBP funding policy. The stated intent of the QBP has been to drive improved efficiency by uisng a fixed price across all cases based on the 40th percentile of patient costs, and to further incentivize the continued shift to outpatient rehabilitation.

Notwithstanding these efforts, a number of areas for improvement in the provision of primary joint replacement care in Ontario remain. Experts have cited a wide variation in the use of different prostheses types across Ontario hospitals, with more expensive devices often used without a clear association with patient characteristics, which is consistent with similar findings in the United States. (34) The Q3 2012/2013 Orthopaedic Quality Scorecard founds that rates of 30-day readmission vary from 1.2% to 6.6% across higher volume hospitals and between 1.6% and 5.1% across LHINs (33); such regional variation in outcomes suggests possible opportunities for improvement.

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§Calculated based on differences in episode of care costs estimated by Mahomed et al. ((23;27) and current provincial procedure volumes. (23;27)

Finally, there is a need to further develop and leverage the evidence around the impact of patient characteristics on joint replacement care pathways and utilization trajectories. International and Ontario evidence shows that characteristics such as function and comorbidities can drive variations in LOS, costs, and need for inpatient rehabilitation (35-38) as well as in outcomes (35;38-40). Analyzing these factors will support the development of more appropriate and more clinically homogenous care pathways, performance indicators, and funding methodologies.

Primary Hip and Knee Replacement Cohort Definition

Health Quality Ontario (HQO) was tasked with establishing a definition for the primary joint replacement patient cohort (including both hip and knee replacement patients) that consisted of inclusion and exclusion criteria using data elements routinely recorded in Ontario hospital administrative datasets. In order to inform their recommended cohort, HQO worked with the Expert Advisory Panel on Episode of Care for Primary Hip and Knee Replacements Presenting to Hospital (Expert Panel) to review other joint replacement population definitions in current use in provincial applications, including the cohort definition used for funding in the Ministry's current QBP methodology and the cohort definition used in the Orthopaedic Quality Scorecard for Joint Replacement Surgery. The Expert Panel also reviewed a range of analyses drawn from administrative data to inform their deliberations, including lists of CIHI procedure codes (Tables 1 and 2) and descriptive data on the characteristics of the joint replacement population (Tables 3, 6-13). These descriptive analyses frequently stratified patients by different characteristics such as diagnosis and procedure codes and assessed demographic and utilization information for each strata, including average age, acute length of stay, and Health-Based Allocation Model Inpatient Grouper Weight (HIG Weight), a standardized measurement unit of expected cost adjusted for a range of patient and utilization variables.

A common element of all primary hip and knee replacement cohort definitions is their procedure-based inclusion criteria. As an elective surgical procedure, primary hip and knee replacement cases are chiefly identified in hospital administrative data by the presence of a procedure code designating the presence of either a hip or knee replacement intervention in the patient discharge abstract.

While the key inclusion criteria are procedure-based, the majority of primary hip and knee replacement procedures are also performed for a similar diagnosis, namely the treatment of osteoarthritis: as Table 3 illustrates, approximately 92% of the 11,620 primary unilateral hip replacements and 96.5% of the 21,466 primary unilateral knee replacements performed in 2011/2012 in Ontario were recorded with an osteoarthritis-related MRDx code, such as "coxarthrosis unspecified" and "primary coxarthrosis" for hip replacement, or "gonarthrosis unspecified" and "primary gonarthrosis bilateral" for knee replacement. The remaining 8% of hip replacements and 3.5% of knee replacements are made up of a wide variety of low volume MRDx codes, including osteonecrosis (222 cases) and "rheumatoid arthritis unspecified" (125 cases).

Although the scope of the episode of care selected by the Expert Panel for their analysis (see section "Scope of the Primary Hip and Knee Replacement Episode of Care") begins before the patient's actual admission to hospital for surgery, commencing at the referral for an orthopedic hip or knee consultation, the Expert Panel's recommendations apply mainly to cases that are eventually admitted to hospital for surgery; cases that do not receive surgery (e.g., patients that are referred for an orthopedic consultation but are subsequently deemed unfit for surgery or elect not to proceed with surgery) are not included within the cohort definition. Hence, for the purposes of this analysis, the episode of care is essentially established by "working backwards" from a hospital discharge that meets the inclusion and exclusion criteria of the cohort definition.

The following describes the key data elements recorded in the acute inpatient DAD that define the recommended inclusion and exclusion criteria for the primary hip and knee replacement cohort:

- **Procedure codes included**
  Include discharges with recorded Canadian Classification of Interventions (CCI) procedure codes 1VA53** for hip replacements (see Table 1) or 1VG53** for knee replacements (see Table 2), excluding primary cement spacer procedures (codes 1.VA.53.LA-SL-N and 1.VG.53.LA-SL-N).

  Rationale: This definition includes both total and partial joint replacements, as well as both unilateral and simultaneous bilateral replacements (i.e., bilateral replacements performed during the same admission). The Expert Panel opted to consider all primary joint replacements, without limiting the cohort to only total joint replacements. The Expert Panel also strongly recommended that simultaneous bilateral joint replacements be considered in this cohort, although they are a group with a relatively small population. The small number of cement spacer procedures excluded from the cohort (27 and 16 cases recorded for primary hip and knee replacements, respectively, in 2011/2012) are generally performed in cases of revision surgery (e.g., in cases of infected prior joint replacements), and it was suggested that these were unlikely to take place as an independent "primary" operation.

Table 1. Canadian Classification of Interventions Procedure Codes for Hip Replacement

CCI Code	Procedure Description
1VA53LAPM	Single component prosthetic hip open approach (uncemented)
1VA53LAPMA	Single component prosthetic hip open approach using bone autograph (uncemented)
1VA53LAPMK	Single component prosthetic hip open approach using bone homograph (uncemented)
1VA53LAPMN	Single component prosthetic hip open approach with synthetic material
1VA53LAPMQ	Single component prosthetic hip open approach with combined sources of tissue
1VA53LAPN	Dual component prosthetic hip open approach
1VA53LAPNA	Dual component prosthetic hip open approach with autograft
1VA53LAPNK	Dual component prosthetic hip open approach with homograft
1VA53LAPNN	Dual component prosthetic hip open approach with synthetic material
1VA53LAPNQ	Dual component prosthetic hip open approach with combined sources of tissue
1VA53PNPMN	Single component prosthetic hip robotic open approach with synthetic material
1VA53PNPN	Dual component prosthetic hip robotic open approach
1VA53PNPNN	Dual component prosthetic hip robotic open approach with synthetic material

Source: Canadian Classification of Health Interventions 3rd Edition – 2012 CIHI

Table 2. Canadian Classification of Interventions Procedure Codes for Knee Replacement

CCI Code	Procedure Description
1VG53LAPM	Single component prosthetic knee open approach
1VG53LAPMA	Single component prosthetic knee open approach with bone autograft
1VG53LAPMK	Single component prosthetic knee open approach with bone homograft
1VG53LAPMN	Single component prosthetic knee open approach with synthetic material
1VG53LAPMQ	Single component prosthetic knee open approach with combined sources of tissue
1VG53LAPN	Dual component prosthetic knee open approach
1VG53LAPNA	Dual component prosthetic knee open approach with autograft
1VG53LAPNK	Dual component prosthetic knee open approach with homograft
1VG53LAPNN	Dual component prosthetic knee open approach with synthetic material
1VG53LAPNQ	Dual component prosthetic knee open approach with combined sources of tissue
1VG53LAPP	Tri component prosthetic knee open approach
1VG53LAPPA	Tri component prosthetic knee open approach with autograft
1VG53LAPPK	Tri component prosthetic knee open approach with homograft
1VG53LAPPN	Tri component prosthetic knee open approach with synthetic material
1VG53LAPPQ	Tri component prosthetic knee open approach with combined sources of tissue

Source: Canadian Classification of Health Interventions 3rd Edition – 2012 CIHI

- **Admission categories included**
  Include elective cases only (Admission Category = 'L').

  Rationale: This analysis focuses on elective surgeries only. Excluding non-elective hip and knee replacement admissions removes about 5,000 cases, mostly made up of hip fractures and other trauma-related cases.
- **Age range included**
  Include patients aged 18 years or older at admission to hospital only.

  Rationale: The Expert Panel opted to consider only adult cases as part of the episode of care analysis. The small number of pediatric joint replacements conducted in Ontario tend to have significantly different clinical pathways from the adult cases.
- **Intervention attributes included**
  Include primary joint replacements only – exclude cases with attribute "Revision."

  Rationale: The focus of the Expert Panel is on primary joint replacements; revision surgeries are a clinically different patient population and are not included within the mandate of this analysis.

Diagnoses excluded

Exclude cases with a recorded MRDx of cancer-related diagnoses (ICD-10-CA of C** or D** recorded as MRDx) or trauma-related diagnoses (ICD-10-CA of S00** - T32** recorded as MRDx).

Rationale: The relatively few joint replacement cases with an MRDx of cancer (approximately 110 cases in 2011/2012) are likely to follow a significantly different clinical pathway to the general joint replacement population and may be undergoing surgery for treatment of the cancer rather than typical arthritis-related conditions. Before applying the other exclusions above, there were about 6,000 primary joint replacement cases in 2011/2012 with a trauma-related MRDx, but

nearly all of these (mostly hip fracture cases) are already removed from the cohort through the exclusion of non-elective admissions.

- **Transferred cases (episode building)**
  The cohort definition includes prior hospital admissions that are transferred to a different hospital for primary joint replacement surgery as part of the same episode of care, linked back to the index admission.

  Rationale: The scope of the episode of care analyzed through this work (see section Scope of the Primary Hip and Knee Replacement Episode of Care) includes all of a joint replacement patient's prior hospital admissions that are directly related to the subsequent joint replacement.

Recommended Primary Hip and Knee Replacement Patient Groups

The Expert Panel recommended that the overall primary joint replacement population be subdivided into 3 major patient groups based on the type of procedure performed:

- **Group #1:** Patients undergoing primary unilateral hip replacement
- **Group #2:** Patients undergoing primary unilateral knee replacement
- **Group #3:** Patients undergoing simultaneous bilateral primary joint replacements, i.e., replacement of either both knee joints or both hip joints during the same admission

The following determine the inclusion and exclusion criteria for each of the 3 patient groups, based on data elements recorded in the DAD:

- Primary unilateral hip replacement
  - Cases with CCI codes 1.VA.53.**
  - Unilateral replacements only (intervention location attribute = 'L' or 'R')
  - All other criteria are the same as described in the cohort definition

- Primary unilateral knee replacement
  - Cases with CCI codes 1.VG.53.** (unilateral)
  - Unilateral replacements only (intervention location attribute = 'L' or 'R')
  - All other criteria are the same as described in the cohort definition

- Primary bilateral joint replacements
  - Cases with CCI codes for either 1.VA.53.** or 1.VG.53.**
  - Bilateral replacement performed during the same admission (intervention location attribute = 'B')
  - All other criteria are the same as described in the cohort definition

  Rationale: As the 2 major types of primary joint replacement operations, unilateral hip replacements and unilateral knee replacements—while sharing similar diagnoses and similar processes in their overall care pathways—are performed on distinct parts of the anatomy and utilize

distinct types of prostheses. Rehabilitation utilization patterns also tend to vary between the 2 types of joint replacement, as well as patients' trajectories of long-term functional recovery (41).

With only 508 cases performed in Ontario in 2011/2012, simultaneous primary bilateral joint replacements make up only 1.51% of the primary joint replacement population (see Table 3). Of these, approximately 90% are bilateral knee replacements. While making up a small proportion of the overall primary joint replacement population, bilateral replacements have significantly different care pathways and utilization trajectories than unilateral replacements, with each case requiring an additional implant during the same admission, more operating room time, and typically, more time for recovery and rehabilitation than unilateral replacements (also see "Multiple Regression Analysis of Ontario Administrative Data" section). Hence, the Expert Panel recommended that simultaneous bilateral replacements be considered as a distinct third patient group. Because bilateral hip replacements make up a very small proportion of this group, it was recommended that both bilateral hip and knee replacements be combined as a single group.

Primary Hip and Knee Replacement Cohort Descriptive Statistics

Table 3. Primary Joint Replacement Descriptive Statistics

	Patient Group		
	Hip Replacement	**Knee Replacement**	**Bilateral Replacement**
Patient counts			
2011/12 inpatient discharges, n	11,620	21,466	508
Females, n (%)	6,349 (54.6)	13,252 (61.7)	302 (59.4)
Males, n (%)	5,271 (45.4)	8,124 (38.3)	206 (40.6)
Age distribution			
Mean age , year	66.8	67.4	64.7
≤ 49, n (%)	874 (7.5)	668 (3.1)	34 (6.7)
50–64, n (%)	3,902 (33.6)	7,766 (36.2)	216 (42.5)
65–74, n (%)	3,615 (31.1)	7,432 (34.6)	161 (31.6)
≥ 75, n (%)	3,229 (27.8)	5,601 (26.1)	98 (19.2)
Charlson comorbidity score			
0, n (%)	10,447 (89.91)	19,271 (98.78)	Included within hip and knee replacement cohorts for this part of analysis
1–2, n (%)	1,097 (9.44)	2,094 (9.76)	
3+ , n (%)	76 (0.65)	101 (0.47)	
Most responsible diagnosis			
Osteoarthritis unspecified, n (%)	6,584 (56.66)	11,848 (55.19)	46 (9.06)
Primary osteoarthritis bilateral, n (%)	1,823 (15.69)	5,015 (23.36)	383 (75.39)
Other osteoarthritis bilateral, n (%)	2,282 (19.64)	3,846 (17.92)	N/A
Other MRDx, n (%)	931 (8.01)	757 (3.53)	79 (15.55)
Acute inpatient LOS and utilization			
Average LOS, days	4.6	4.2	6.1
Median LOS, days	4	4	4.75
Average ALC LOS, days	0.2	0.1	0.3
Average HIG weight	1.73	1.54	2.54

Comparing the Recommended Cohort Definition with the Ministry's Primary Hip and Knee Replacement Quality-Based Procedure Cohort Definition

The primary hip and knee replacement cohort definition recommended by the Expert Panel is very similar to the cohort definition used by the Ministry for the 2012/2013 QBP funding methodology (see Figure 1), with the notable exception that the Expert Panel included simultaneous bilateral procedures, previously excluded from the QBP definition.

Following their review of the Expert Panel's recommended cohort definition, the Ministry proposed that the cohort be revised slightly to exclude cases that are not included in the corresponding HIG definitions for primary unilateral hip replacement, primary unilateral knee replacement and bilateral joint replacement, as follows:

1. For the Unilateral Hip Replacement patient group, exclude cases not included in HIG 320
2. For the Unilateral Knee Replacement patient group, exclude cases not included in HIG 321
3. For the Simultaneous Bilateral Replacement patient group, exclude cases not included in HIG 315

Cases included in the Expert Panel's cohort definition that are not also included in these HIGs are small in number (consisting of 90 cases for unilateral hip replacement, 114 cases for unilateral knee replacement and 1 case for simultaneous bilateral joint replacement in 2011/2012) and tend to include other major surgeries such as pacemaker implantations or colostomies that would typically assign these cases to other case mix groups (and potentially QBPs) rather than joint replacement. These cases also tend to have considerably longer lengths of stay and higher RIW values.

Scope of the Primary Hip and Knee Replacement Episode of Care

The Expert Panel defined a scope for the episode of care for this analysis somewhat differently from previous episode of care analyses. The Expert Panel strongly believed that this work should consider not just perioperative care, but also the care involved before and after the hospital admission, including the patient's referral from a primary care provider for a hip or knee orthopedic consultation ('Wait 1'), the period between the decision to treat and the admission for surgery ('Wait 2'), and post-acute care and rehabilitation following discharge from acute care.

It should be noted that although the proposed episode scope begins at referral for an orthopedic consultation, the Expert Panel's recommendations apply to cases that are eventually admitted to hospital for surgery; cases that do not receive surgery (e.g., patients who are referred for an orthopedic consultation but are subsequently deemed unfit for surgery or elect not to proceed with surgery) are not included within the cohort definition. Hence, for the purposes of this analysis, the episode of care is essentially established by "working backwards" from a hospital discharge that meets the inclusion and exclusion criteria of the cohort definition.

Post-acute care plays a key role in high quality joint replacement care. Studies in Ontario (24) and the United States (42) have confirmed that a major chunk of total utilization related to joint replacement occurs in the period following discharge from acute care, including rehabilitation, follow-up physician

services, and for 3.1% of patients in Ontario (Q3 2012/2013), unplanned readmissions to hospital within 30 days of discharge (33). Hence, similar to the recommended scope of HQO's previous Hip Fracture analysis, the Expert Panel strongly believed that the episode of care analyzed here and any future applications of this work should capture an appropriate period of relevant health care activity following discharge from acute care. Previous research in Ontario has revealed striking regional variation in discharge practice following joint replacement surgery (24;43).

In deciding on the appropriate post-acute time window to adopt for the episode definition, the Expert Panel considered several options. A period of 30 days following discharge from acute care was felt to be insufficient for comprehensively capturing relevant post-acute rehabilitation and home care services for many patients. The duration of post-acute home care services received by primary joint replacement patients across the province in 2011/2012 averaged 51.4 days (median: 42 days) for hip replacement (see Table 4) and 39.7 days (median: 32 days) for knee replacement (see Table 5). The Expert Panel ultimately agreed that a 90-day window of time following discharge from acute care was likely to be sufficient for capturing the majority of this utilization.

Table 4. Duration of Post-Acute Home Care Services for Hip Replacement Patients (2011/2012)

LHIN	Total Cases,	Home Care Within 90 days				Days of Post-Acute Home Care Services	
		No		Yes		Mean	Median
	n	n	%	n	%		
ONTARIO	11100	5986	53.9	5114	46.1	51.4	42
Erie St. Clair	657	261	39.7	396	60.3	39.7	24
South West	991	688	69.4	303	30.6	39.1	23
Waterloo Wellington	628	488	77.7	140	22.3	57.1	41
Hamilton Niagara Haldimand Brant	1478	427	28.9	1051	71.1	47.2	42
Central West	352	116	33.0	236	67.0	51.2	45
Mississauga Halton	791	175	22.1	616	77.9	48.3	44
Toronto Central	804	463	57.6	341	42.4	53.9	44
Central	1012	510	50.4	502	49.6	65.5	53
Central East	1200	735	61.3	465	38.8	50.5	39
South East	534	350	65.5	184	34.5	56.9	48
Champlain	1149	746	64.9	403	35.1	55.6	44
North Simcoe Muskoka	478	357	74.7	121	25.3	52.7	52
North East	661	484	73.2	177	26.8	74.1	53
North West	284	131	46.1	153	53.9	50.5	46
Unknown	**81**	**55**	**67.9**	**26**	**32.1**		

Source: Discharge Abstract Database and Home Care Database (2011/2012)

Table 5. Duration of post-acute home care services for knee replacement patients (2011/2012)

LHIN	All Cases	Home Care Within 90 days				Days of Post-Acute Home Care Services	
		No		Yes		Mean	Median
	n	n	%	n	%		
ONTARIO	20864	12965	62.1	7899	37.9	39.7	32
Erie St. Clair	1144	499	43.6	645	56.4	21.7	15
South West	1768	1306	73.9	462	26.1	29.6	18
Waterloo Wellington	1032	849	82.3	183	17.7	47.9	36
Hamilton Niagara Haldimand Brant	2824	894	31.7	1930	68.3	36.0	33
Central West	1159	633	54.6	526	45.4	41.8	35
Mississauga Halton	1315	439	33.4	876	66.6	37.2	34
Toronto Central	1097	723	65.9	374	34.1	55.2	42
Central	1925	1340	69.6	585	30.4	58.3	43
Central East	2379	1753	73.7	626	26.3	46.6	36
South East	1108	746	67.3	362	32.7	37.5	34
Champlain	2131	1649	77.4	482	22.6	41.4	26
North Simcoe Muskoka	848	674	79.5	174	20.5	42.7	37
North East	1500	1024	68.3	476	31.7	46.7	37
North West	473	304	64.3	169	35.7	30.8	11
Unknown	**161**	**132**	**82.0**	**29**	**18.0**		

Source: Discharge Abstract Database and Home Care Database (2011/2012)

Key Parameters Recommended for the Episode of Care

Applying the key parameters required to define and episode of care articulated by Averill et al, (1) Hussey et al, (2) and Rosen and Borzecki (3) (see the "Methods" section), the Expert Panel defined the scope of analysis for the primary hip and knee replacement episode of care as follows:

- **Index event:** A patient's initial referral from primary care for a hip or knee consultation, provided that the patient is subsequently discharged following primary hip or knee replacement surgery and fits the inclusion and exclusion criteria in the cohort definition above (see "Primary Hip and Knee Replacement Cohort Definition"). Any related hospital admissions (i.e., transfers) prior to the patient's admission for the surgery are linked with the surgical admission and included within the same episode of care.
- **Endpoint:** The primary hip and knee replacement episode of care concludes at either 90 days following discharge from the surgical acute care stay or death.
- **Types of services included:** The Expert Panel recommended that analysis be limited to health care services. Non-health care services such as social care services are not included, and are likely not to be relevant to this analysis for the majority of this population.

Analysis of Primary Hip and Knee Replacement Patient Characteristics

Although the set of 3 patient groups recommended by the Expert Panel is a simple and clinically intuitive approach to grouping the primary joint replacement patient population, classifying patients according to whether they received a hip or knee procedure does little to explain significant variations in the trajectory of care and utilization observed among patients. Within each patient group, varying proportions of patients will receive additional diagnostic tests, additional specialist consultations, have a greater propensity to be admitted to a critical care unit or be discharged to an inpatient rehabilitation setting rather than an outpatient rehabilitation program, may require a longer LOS in either acute care or rehabilitation, may require more costly components of care (such as implants that are more expensive due to specific clinical properties) or incur higher overall costs. While some portion of this variation in practice is driven by hospital or surgeon-specific factors—what might be considered to be variation in quality and efficiency—a significant share of variation in practice is attributable to differences in baseline (pre-admission) patient characteristics such as a patient's age, major diagnosis, and comorbidities.

Hence, given their mandate of defining clinically homogenous groupings and care pathways for the primary hip and knee replacement population, the Expert Panel considered a range of patient characteristics that are associated with appropriate variations in care provided for this population. In particular, the Expert Panel sought to make recommendations on the patient characteristics that evidence and clinical experience suggest have the greatest impact in driving variations in clinical practice and utilization for primary hip and knee replacement. The scientific literature suggests that a number of the same factors associated with variations in the care pathways of joint replacement patients—such as comorbidity burden—are also associated with variation in patient outcomes such as mortality, complication rates, readmissions, and patient satisfaction.

The Expert Panel reviewed several different varieties of evidence to support their analysis of patient characteristics, with a focus on utilization-related outcomes (such as LOS, use of particular health services, and cost) as these were seen to be the closest proxies for variations in care pathways:

- **A literature review** of studies examining the association between primary hip and knee replacement patient characteristics and outcomes such as acute care LOS, rehabilitation LOS, utilization of particular interventions (such as critical care units and inpatient rehabilitation), costs, and complications
- **Descriptive analysis** of Ontario administrative data, analyzing LOS and HIG weights for subgroups of the joint replacement population stratified by patient characteristics
- **Multivariate analysis** of Ontario administrative data, regressing outcomes of acute LOS and acute care cost on a set of patient characteristics recommended by the Expert Panel based on their review of the literature and descriptive analysis, clinical experience, and the availability of these characteristics within current administrative data

These analyses and related conclusions and recommendations are presented in the following section. The results have implications for applications including: assigning patients to the appropriate clinical pathway, evaluating the effectiveness of specific interventions within homogenous subgroups (e.g., assessing the value of pre-operative screening in "healthy" versus comorbid patients), classifying patients according to their expected cost and resource utilization for the purposes of the QBP funding methodology, and applying appropriate risk adjustment methodologies for performance indicators and target-setting under the QBP Integrated Scorecard.

Literature Review on the Effect of Primary Hip and Knee Replacement Patient Characteristics

The scientific literature identifies a number of patient characteristics associated with variation in hip and knee replacement care pathways and corresponding measures of utilization:

Patient characteristics currently available in Ontario hospital administrative data:

- **Age:** Kreder et al (38) found that for total knee arthroplasty, each additional 10 years of age is associated with an increase in acute LOS of 0.7 days, as well as higher risks of in-hospital complications and 3 month mortality. Husted et al (35) found a positive relationship for both total hip and knee replacement patients between increasing age and increasing LOS. Kim (44) found a 'U-shaped' relationship between age and cost for both total hip and knee arthroplasty, where age under 45 years and above 75 years were associated with greater hospital costs than ages 45 to 75 years. Tien et al (45) similarly found that age under 45 years was associated with increased hospital costs for both hip and knee replacement patients. Memtsoudis et al (46) found that increasing age was associated with greater risk of using critical care services in a total joint replacement population. Reuben et al (47) found an inverse relationship between age and total costs for primary knee replacement, but found no significant relationship for primary hip replacement.
- **Sex:** In studies examining total knee replacement populations, Kim (44) and Reuben et al (47) both found that male sex was associated with slightly increased hospital costs, while Kreder et al (38) found that female sex was associated with a 0.4 day increase in acute LOS. Husted et al (35) found that female sex was associated with longer LOS in a combined total joint replacement population. Tien et al (45) found that male sex was associated with increased hospital costs for primary hip replacement. Lin and Kaplan (36) found that male sex was associated with longer inpatient rehabilitation lengths of stay for all joint replacements. Memtsoudis et al (46) found that male sex was associated with a greater risk for requiring critical care services in both joint replacement patient groups.
- **Primary diagnosis:** While studies in several jurisdictions have found osteoarthritis to be the primary diagnosis for over 90% of total joint replacement patients (5;45;48), Tien et al (45) and Ilfield et al (49) found that non-osteoarthritis primary diagnoses were associated with longer LOS and higher hospital costs. Memtsoudis et al (46) found that non-osteoarthritis primary diagnoses were also associated with a greater risk of need for critical care services.
- **Comorbidity:** Kreder et al (38), studying a total knee replacement population, found that a Charlson comorbidity score of 1 was associated with an increase in acute LOS of 0.9 days while a Charlson score of more than 1 was associated with an acute LOS increase of 2.8 days (both effects in comparison with Charlson score of 0). A higher Charlson score was also associated with greater risk of 3-month mortality. Tien et al (45) also found that a higher Charlson score was associated with higher hospital costs for both hip and knee replacement patients. Reuben et al (47) found that a higher American Society of Anesthesiologists (ASA) score was associated with higher costs for both joint replacement populations, while Husted et al (35) found that higher ASA was associated with longer LOS for both joint replacements. Studying a combined joint replacement population, Lin and Kaplan (36) found that each additional comorbid illness was associated with a 0.56 day increase in inpatient rehabilitation LOS. Memtsoudis et al (46) analyzed a range of comorbidities in a total joint replacement population and found that all conditions except rheumatic disease were associated with increased risk of requiring critical care

services, with renal disease, liver disease, dementia, and cerebrovascular disease having the greatest risk.

- **Bilateral replacements:** Reuben et al (47) compared the costs of unilateral and bilateral joint replacements and found that simultaneous sequential bilateral joint arthroplasties—while more costly than a single unilateral replacement—were more cost-effective than staged bilateral joint arthroplasty or 2 primary unilateral surgeries.

Patient characteristics currently absent in Ontario hospital administrative data:

- **Obesity:** Both Kim (44) and Silber et al (50) found that Body Mass Index (BMI) ranges classified as obese and morbidly obese were associated with progressively higher hospital costs for both total hip and knee arthroplasty patients.
- **Ethnicity:** Kim (44) found that non-white ethnicity was associated with significantly greater hospital costs for both hip and knee replacements, while Lin and Kaplan (36) found that black race was associated with longer LOS in inpatient rehabilitation for both joint replacements.
- **Marital status:** Studies have found that marital status has a significant association with LOS: Husted et al (35) found that patients living alone were at higher risk for longer acute LOS, while Lin and Kaplan (36) found that unmarried status was associated with a 1.19 day increase in inpatient rehabilitation LOS.

Descriptive Analysis of Ontario Administrative Data for Primary Hip and Knee Replacement Subgroups Stratified by Patient Characteristics

The Expert Panel reviewed the following analyses to support their discussion on an appropriate approach towards stratifying the hip and knee replacement population:

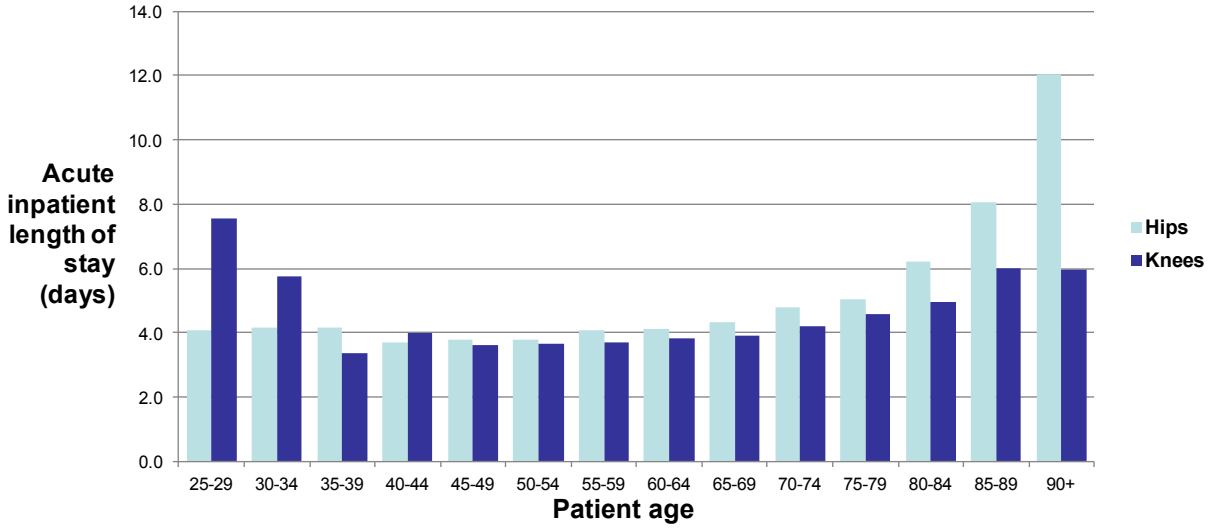


Figure 6. Hip and Knee Replacement Acute Length of Stay by Age Group

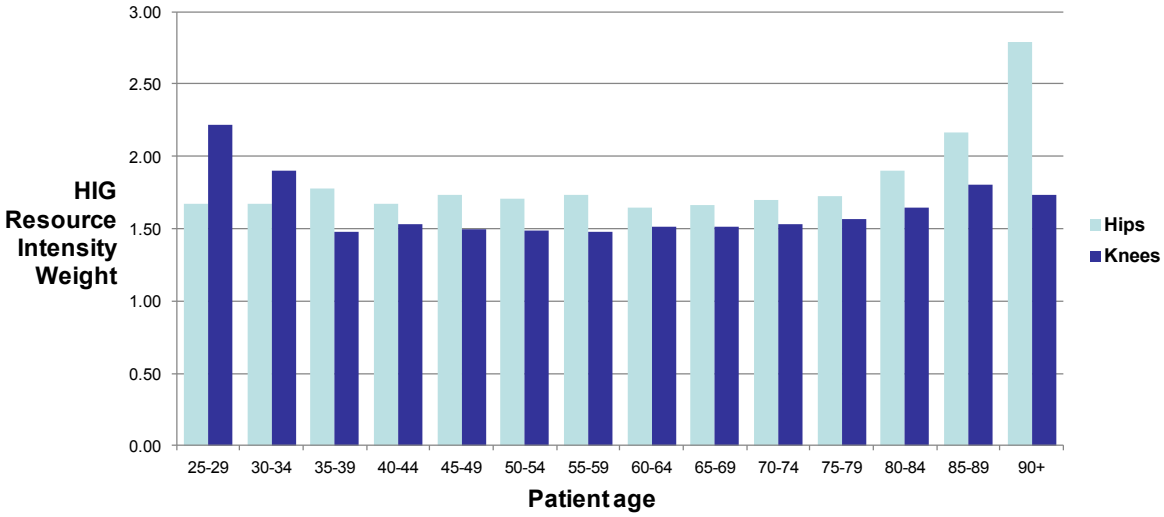


Figure 7. Hip and Knee Replacement HIG Resource Intensity Weight by Age Group

Table 6. Primary Joint Replacement Patients by Age and Sex

Age Group, years	Sex	Cases, n	Average LOS, days	Average HIG Weight
20–29	FEMALE	31	4.3	1.67
	MALE	38	4.3	1.95
30–39	FEMALE	83	4.0	1.64
	MALE	97	4.1	1.74
40–49	FEMALE	652	3.8	1.60
	MALE	651	3.5	1.65
50–59	FEMALE	3,670	3.9	1.56
	MALE	2,739	3.6	1.61
60–69	FEMALE	6,742	4.1	1.57
	MALE	4,597	3.9	1.59
70–79	FEMALE	6,081	4.6	1.61
	MALE	4,016	4.5	1.65
80–89	FEMALE	2,535	5.5	1.76
	MALE	1,499	5.8	1.83
90+	FEMALE	107	7.5	2.10
	MALE	50	8.6	2.14

Source: Discharge Abstract Database (2011/2012).

Table 7. Primary Unilateral Hip Replacements by Most Responsible Diagnosis

	Most Responsible Diagnosis	Number of cases, n	Total cases, %	Average LOS	Average HIG Weight	Average age, years
M169	Coxarthrosis unspecified	6,584	56.19	4.5	1.68	68
M161	Other primary coxarthrosis	2,282	19.47	4.3	1.68	67
M160	Primary coxarthrosis bilateral	1,823	15.56	4.3	1.68	67
M8795	Unspecified osteonecrosis pelvis thigh	222	1.89	5.9	1.94	59
M165	Other post-traumatic coxarthrosis	116	0.99	4.8	1.77	60
M167	Other secondary coxarthrosis	79	0.67	4.2	1.72	55
M163	Other dysplastic coxarthrosis	64	0.55	4.3	1.69	55
T8413	Mech comp of int fix device of femur	59	0.50	12.4	2.77	78
M069	Rheumatoid arthritis unspecified	58	0.49	5.1	1.84	63
M8415	Nonunion fx [pseudarthrosis] pelvis thigh	39	0.33	7.9	2.16	67
C795	Sec malgt neoplasm bone & bone marrow	38	0.32	17.8	3.53	66
M166	Other secondary coxarthrosis bilateral	34	0.29	4.5	1.80	58
M8715	Osteonecrosis due to drugs pelvis thigh	22	0.19	3.7	1.65	47
M8445	Pathological fracture NEC pelvis thigh	20	0.17	13.4	3.04	73
M8705	Idiopath aseptic necrosis bone pelv thigh	19	0.16	5.7	1.89	60
M8725	Osteonecrosis dt prev trauma pelv thigh	18	0.15	10.4	2.72	64
M1395	Arthritis unspecified pelvis & thigh	15	0.13	5.6	1.79	69
M162	Bil coxarthrosis result from dysplasia	12	0.10	3.5	1.67	48
C900	Multiple myeloma	9	0.08	15.6	3.40	71
M8095	Osteoporosis NOS w path fx pelvis thigh	9	0.08	17.2	3.31	81
	All other diagnoses	196	1.67	16.2	3.66	62
	All cases			5.9	1.92	67

Source: Discharge Abstract Database (2011/2012).

Table 8. Primary unilateral knee replacements by Most Responsible Diagnosis

	Most Responsible Diagnosis	Number of cases, n	Percentage of total cases	Average LOS, days	Average HIG Weight	Average age, years
M179	Gonarthrosis unspecified	11,848	55.40	4.2	1.53	68
M170	Primary gonarthrosis bilateral	5,015	23.45	4.0	1.53	68
M171	Other primary gonarthrosis	3,846	17.98	4.2	1.54	67
M173	Other post-traumatic gonarthrosis	192	0.90	4.0	1.53	60
M175	Other secondary gonarthrosis	143	0.67	4.3	1.52	66
M069	Rheumatoid arthritis unspecified	125	0.58	4.3	1.55	62
M174	Other secondary gonarthrosis bilateral	44	0.21	4.3	1.50	68
M1396	Arthritis unspecified lower leg	30	0.14	4.4	1.54	62
M172	Post-traumatic gonarthrosis bilateral	21	0.10	4.3	1.52	60
M8796	Unspecified osteonecrosis lower leg	16	0.07	3.4	1.48	67
T848	Oth comp int ortho prosth dev impl gft	9	0.04	7.1	1.98	63
L405	Arthropathic psoriasis	7	0.03	4.1	1.47	62
M0096	Pyogenic arthritis NOS lower leg	7	0.03	11.0	2.38	59
T8454	Infect & infl reaction dt knee prosth	6	0.03	11.5	2.58	76
M068	Other specified rheumatoid arthritis	5	0.02	3.6	1.46	50
M199	Arthrosis, unspecified	5	0.02	2.8	1.49	68
M080	Juvenile rheumatoid arthritis	4	0.02	5.8	1.42	56
M8786	Other osteonecrosis lower leg	4	0.02	3.3	1.47	68
M1386	Other specified arthritis lower leg	3	0.01	3.7	1.47	64
M150	Primary generalized (osteo)arthrosis	3	0.01	3.7	1.47	63
	All other diagnoses	52	0.24	7.7	2.14	61
	All cases			4.1	1.54	67

Source: Discharge Abstract Database (2011/2012).

Table 9. Primary Unilateral Hip Replacement by Primary Procedure

Procedure		Percentage of total	Total Cost Per Case, $		LOS, days	
			Average	SD	Average	SD
1VA53LAPNA	Implant dual comp prosth hip OA &autogr	46.92	9,960	9,796	4.9	5.6
1VA53LAPN	Implant dual comp prosth hip OA	35.48	9,696	4,071	4.5	4.3
1VA53LAPNN	Implant dual comp prosth hip OA &synth mat	9.02	11,219	7,836	5.3	5.5
1VA53LAPNQ	Implant dual comp prosth hip OA &combo tis	5.29	11,298	7,350	6.3	9.2
1VA53LAPNK	Implant dual comp prosth hip OA &homogr	0.95	10,125	2,382	4.5	2.0
1VA53LAPM	Implant sing comp prosth hip OA	0.73	13,065	8,548	10.3	16.8
1VA53LAPMN	Implant sing comp prosth hip OA &synth mat	0.70	15,054	9,850	10.3	16.5
1VA53LAPMA	Implant sing comp prosth hip OA &autogr	0.64	10,789	3,308	5.2	4.1
1VA53LAPMQ	Implant sing comp prosth hip OA &combo tis	0.15	9,683	1,868	3.5	1.8
1VA53LASLN	Implant dev hip OA &spacer synth mater	0.12	34,487	34,732	29.7	36.6

Abbreviation: SD, standard deviation.
Source: Discharge Abstract Database (2011/2012).

Table 10. Primary Unilateral Knee Replacement by Primary Procedure

Procedure		Percentage of all cases	Total Cost Per Case, $		LOS, days	
			Average	SD	Average	SD
1VG53LAPPQ	Implant tri comp prosth knee OA &comb tis	43.68	9,046	3,033	4.5	2.6
1VG53LAPPN	Implant tri comp prosth knee OA &synth mat	28.07	8,495	3,266	4.4	2.6
1VG53LAPNQ	Implant dual comp prosth knee OA &comb tis	11.11	8,587	2,898	4.5	2.8
1VG53LAPNN	Implant dual comp prosth knee OA &synth mat	9.56	8,720	2,923	4.3	2.4
1VG53LAPNA	Implant dual comp prosth knee OA &autogr	1.79	8,478	1,985	4.7	1.8
1VG53LAPPA	Implant tri comp prosth knee OA &autogr	1.55	9,533	2,456	4.7	2.0
1VG53LAPP	Implant tri comp prosth knee OA	1.51	8,976	2,505	4.3	2.4
1VG53LAPN	Implant dual comp prosth knee OA	1.17	9,516	8,508	4.2	6.1
1VG53LAPMN	Implant sing comp prosth knee OA &syn mat	0.48	8,669	1,658	3.4	1.1
1VG53LAPMQ	Implant sing comp prosth knee OA &comb tis	0.34	9,103	1,933	4.5	2.0
1VP53LAPMN	Implant dev patella OA &prosthesis synth mater	0.29	7,963	2,052	3.0	1.3
1VG53LASLN	Implant cement spacer knee OA	0.20	11,648	6,975	6.7	5.5
1VG53LAPM	Implant sing comp prosth knee OA	0.16	9,125	4,440	4.8	6.0
1VG53LAPPK	Implant tri comp prosth knee OA &homogr	0.10	9,430	1,839	4.3	1.6

Abbreviation: SD, standard deviation.
Source: Ontario Case Costing Initiative (2010/2011).

Table 11. Primary Unilateral Hip and Knee Replacements by Comorbidity Score[a]

Comorbidity score	Percent of total population	Average acute care cost, $	Average acute care LOS, days
Hip replacement			
0	89.91	9,935.40	4.2
1	9.44	11,550.66	5.4
≥ 2	0.65	13,793.61	6.4
Knee replacement			
0	89.77	8,857.17	4
1	9.76	10,106.47	4.7
≥ 2	0.47	13,956.27	6.4

[a]See Table 14 for list of comorbidities included; comorbidity score calculated from diagnoses coded as Type 1 Pre-admit Comorbidity, Type 1 Service Transfer diagnosis and Type 3 Secondary Diagnosis.
Source: Discharge Abstract Database (2011/2012) and Ontario Case Costing Initiative (2011/2012)

Table 12. Primary Unilateral Hip Replacements: Top 25 Primary (Type 1) Comorbidity Diagnoses, by Volume

	Comorbidity diagnosis	Number of cases, n	Percentage of total cases	Average LOS, days	Average HIG Weight
I100	Benign hypertension	168	1.45	7.0	2.08
D649	Anaemia unspecified	156	1.34	7.9	2.26
M8795	Unspecified osteonecrosis pelvis thigh	151	1.30	5.1	1.80
M8565	Other cyst of bone pelvis & thigh	97	0.83	3.7	1.69
I480	Atrial fibrillation	91	0.78	10.5	2.47
Z501	Other physical therapy	84	0.72	4.4	1.70
E119	Type 2 DM no comp	57	0.49	6.4	2.01
M706	Trochanteric bursitis	50	0.43	5.1	1.74
Z507	OT & vocational rehabilitation NEC	45	0.39	4.4	2.01
M169	Coxarthrosis unspecified	44	0.38	8.0	2.56
M6215	Oth rupture muscle (nontraum) pelv thgh	38	0.33	4.6	1.67
M707	Other bursitis of hip	38	0.33	6.4	1.99
G4738	Other sleep apnoea	34	0.29	4.5	1.77
G4730	Sleep apnoea, obstructed	33	0.28	5.3	1.86
M247	Protrusio acetabuli	30	0.26	5.8	1.89
Q658	Other congenital deformities of hip	30	0.26	4.0	1.69
M2585	Other spec joint disorders pelvis thigh	28	0.24	3.9	1.63
N390	Urinary tract infection site not spec	27	0.23	10.9	2.69
M2575	Osteophyte pelvic region and thigh	24	0.21	4.4	1.74
E785	Hyperlipidaemia unspecified	23	0.20	4.8	1.83
E668	Other obesity	22	0.19	5.4	1.85
J449	COPD unspecified	22	0.19	6.0	2.05
M6595	Synovitis tenosynovitis NOS pelvis thgh	22	0.19	5.8	1.98
Z470	F/U care r/o fx plate oth int fix dev	22	0.19	4.5	1.71
M069	Rheumatoid arthritis unspecified	21	0.18	4.8	1.78

Source: Discharge Abstract Database (2011/2012).

Table 13. Primary Unilateral Knee Replacements: Top 25 Primary Comorbidity (Type 1) Diagnoses, by Volume

	Comorbidity diagnosis	Number of cases, n	Percentage of total cases	Average LOS, days	Average HIG Weight
I100	Benign hypertension	387	1.80	5.1	1.64
M211	Varus deformity NEC	375	1.75	3.7	1.51
Z501	Other physical therapy	231	1.08	4.3	1.53
M6596	Synovitis & tenosynovitis NOS lower leg	197	0.92	5.1	1.65
D649	Anaemia unspecified	186	0.87	4.7	1.60
M210	Valgus deformity NEC	119	0.55	3.9	1.50
I480	Atrial fibrillation	115	0.54	7.6	1.96
E119	Type 2 DM no comp	112	0.52	4.6	1.63
G4730	Sleep apnoea, obstructed	105	0.49	5.4	1.72
M704	Prepatellar bursitis	89	0.41	5.3	1.60
G4738	Other sleep apnoea	72	0.34	4.3	1.54
E668	Other obesity	56	0.26	4.9	1.64
M2576	Osteophyte lower leg	51	0.24	3.7	1.52
M069	Rheumatoid arthritis unspecified	48	0.22	4.9	1.63
E1164	Type 2 DM w poor control	47	0.22	5.4	1.66
Z507	OT & vocational rehabilitation NEC	47	0.22	4.3	1.79
M712	Synovial cyst of popliteal space [Baker]	46	0.21	3.9	1.49
M705	Other bursitis of knee	35	0.16	4.9	1.54
M2456	Contracture of joint lower leg	34	0.16	4.2	1.59
E1152	Type 2 DM w certain circ comp	33	0.15	7.8	2.04
M234	Loose body in knee	30	0.14	4.3	1.47
E876	Hypokalaemia	28	0.13	4.9	1.53
E039	Hypothyroidism unspecified	27	0.13	4.6	1.62
N390	Urinary tract infection site not spec	27	0.13	7.3	2.05
J449	COPD unspecified	26	0.12	6.2	1.92

Source: Discharge Abstract Database (2011/2012).

Multiple Regression Analysis of Ontario Administrative Data

Based on their examination of the literature and descriptive analyses and on their clinical experience and intuition, the Expert Panel recommended a set of patient characteristics for further analysis. Similar to the methods used in the Hip Fracture Episode of Care Analysis, HQO worked with the Ministry's Health Analytics Branch to develop multiple regression models to examine the association between these characteristics and key outcomes.

This process of evidence development ensures that patient characteristics identified in the international literature or suggested by Expert Panel members based on their clinical experience are contextualized and assessed with empirical analysis of Ontario administrative data. Using outcome measures that are relevant to intended end purposes of this work (LOS and cost), patient characteristics that can be translated to Ontario administrative data are assessed for the significance, directionality, and magnitude of their associations with these outcomes. The results of the analysis provide a robust set of variables that evidence shows to be relevant for clinical and policy applications such as care pathway development, performance measurement, health care planning, and funding.

It should be noted that the variables modelled here are only those characteristics that can be translated to current Ontario administrative data. The Expert Panel also recommended other patient characteristics be considered including obesity, ASA score, and factors related to patients' social situations such as marital status and availability of caregiver supports. However, these characteristics are not currently captured in routine acute care data and could not be modelled at this time.

Data Sources Used

The cohort studied for this analysis was defined based on the data elements in the Expert Panel's recommended inclusion and exclusion criteria (see the "Primary Hip and Knee Replacement Cohort Definition" section). Two datasets were used for the analysis: DAD records for fiscal year 2011/2012 were used for the analysis of patient factors predicting acute care LOS, while Ontario Case Costing Initiative records for fiscal year 2011/2012 were used for the analysis of patient factors predicting acute care cost. As the OCCI dataset contains patient-level costing data collected through a standard activity-based costing methodology, it was determined that OCCI data would be more suitable for capturing patient-driven heterogeneity in resource utilization than the HIG weights used by the DAD, which tend to compress differences in resource utilization between patients when dealing with clinical populations with a lower percentage of LOS outliers or patients that received complex interventions.

OCCI data is collected from a sample of 45 hospital corporations (out of the approximately 150 total hospital corporations in Ontario) largely made up of large community and teaching hospitals. The OCCI sample is believed to be fairly representative of the total provincial population: OCCI contains records for over half of the total provincial discharges for primary joint replacement recorded in the DAD: 6,191 out of 11,620 (53.3%) hip replacement discharges and 11,163 out of 21,466 (52.0%) knee replacement discharges. There are only a few small hospitals in the dataset; however, there are few small hospitals that perform significant volumes of primary joint replacement.

Dependent Variables

Given time and resource constraints, 2 dependent (outcome) variables were selected for the multivariate analysis:

- **Acute inpatient LOS:** Recorded at the patient level through the DAD, this measure captures total acute LOS and includes ALC days. It does not include days of stay in rehabilitation facilities or the community following acute discharge. LOS is a key component of many clinical care pathways and a key measure of overall utilization and has been the subject of provincial joint replacement performance measures and targets in the past (such as the Orthopaedic Expert Panel's 4.4 day acute LOS target). (31) LOS has also been previously identified by the Ministry as a priority topic for recommendations from the Episode of Care Expert Panels.
- **Acute inpatient cost:** Calculated at the patient level through the OCCI, this measure includes only acute care hospital costs and does not include physician costs or post-acute care costs. While the Expert Panel's mandate did not include detailed costing analysis, patient-level cost provides a comprehensive measure for assessing variations in overall utilization within patient care pathways and is a relevant outcome for a variety of policy and planning applications. It also provides a relevant outcome for potential linkage to future cost-effectiveness analyses (part of HQO's evidence-based analyses product) and OHTAC review.

Independent Variables

The following describes the set of independent (patient characteristic) variables analyzed, the rationale for their inclusion, and the details of their specification in the models:

- **Age:** Identified in numerous studies as a key determinant of care in hip and knee replacement. (35;38;44-47) May affect factors such as choice of implants, diagnostics, and patient recovery time. Some literature has identified a U-shaped relationship between age and utilization, that is, very young and very old joint replacement patients tend to be associated with higher costs and longer LOS. (45)

  Model specification: Dummy variables were included for 4 age categories: ≤ 49 years; 50–64 years; 65–74 years; 75+ years.

- **Sex:** Identified in a number of studies as a predictive variable, although generally of limited magnitude. Male sex tends to be associated with greater costs and LOS and need for specific services (36;44;46;47).
  Model specification: Dummy variables were included for male and female sex.

- **Comorbidity**: Identified as a strong predictor of variation in utilization in numerous studies (35;36;38;45-47), comorbidity has been captured by various different forms in the literature, including being modelled by individual comorbid diseases (46) and through indices measuring overall burden of comorbidity such as the Charlson Comorbidity index (51), which has been used in a number of studies for primary joint replacement (38;45). The Charlson index was endorsed by the Expert Panel and a variation of the index is used for this analysis.

Model specification: 3 dummy variables were included for Comorbidity index score of 0, 1, and 2, representing the following:

- Comorb_index = 0 for all patients with Charlson Comorbidity Index score of 0
- Comorb_index = 1 for all patients with Charlson Comorbidity Index score of 1 or 2
- Comorb_index = 2 for all patients with Charlson Comorbidity Index score greater than 2 (see Table 14 for Charlson Comorbidity Index scores)

The Comorbidity index score was calculated based on the diagnoses in Table 14 being coded in a record as either a Type 1 Pre-admit Comorbidity, Type W, X, Y Service Transfer diagnosis, or Type 3 Secondary Diagnosis.

Table 14. Charlson Comorbidity Index Scores and Corresponding Comorbidity Indexes Allocated

Condition	Points	Comorbidity Index Allocated
Myocardial infarction	1	1
Congestive heart failure	1	1
Peripheral vascular disease	1	1
Cerebrovascular disease	1	1
Dementia	1	1
COPD	1	1
Connective tissue disease	1	1
Peptic ulcer disease	1	1
Diabetes mellitus	1 if uncomplicated, 2 if end-organ damage present	1
Chronic kidney disease	2 if moderate to severe	1
Hemiplegia	2	1
Leukemia	2	1
Malignant lymphoma	2	1
Solid tumour	2; 6 if metastatic	1 or 2
Liver disease	1 if mild; 3 if moderate to severe	1 or 2
AIDS	6	2

Abbreviation: AIDS, acquired immune deficiency syndrome.

Initial analysis presented to the Expert Panel included a Comorbidity Index calculated using only those diagnoses coded as Type 1 and Type W, X, Y diagnosis types. This approach resulted in a very low proportion (fewer than 1.3%) of patients being recorded as having a comorbidity, which the Expert Panel considered as not having face validity. Subsequently, the models were modified to include diagnoses coded as Secondary Diagnosis, resulting in just over 10% of patients being recorded as having a comorbidity.

- **Simultaneous bilateral versus unilateral replacement:** The Expert Panel accepted that simultaneous bilateral replacements (i.e., 2 joints replaced during the same hospital admission) would have greater costs and longer LOS than unilateral replacements due to the cost of an additional prostheses and longer operating room and recovery time required. This relationship has also been demonstrated elsewhere (47). While the Expert Panel recommended that simultaneous

bilateral replacements be considered a separate patient group from unilateral replacements (see "Recommended Hip and Knee Replacement Patient Groups"), it was thought that including them in this analysis might yield some useful estimates of differences in cost and LOS.
Model specification: Dummy variables were included designating the case as a unilateral or simultaneous bilateral replacement (location attribute = 'B').

- **Intervention type:** While some members of the Expert Panel were somewhat skeptical of the face validity of the CCI system for capturing meaningful differences in joint replacement operation types, procedure codes are readily available in the administrative data.
Model specification: Dummy variables for each of the following CCI procedure codes recorded as the Primary Procedure for the case:

  Hip replacement:
  - 1VA53LAPN Dual component prosthetic hip open approach
  - 1VA53LAPNA Dual component prosthetic hip open approach with autograft
  - 1VA53LAPNN Dual component prosthetic hip open approach with synthetic material
  - 1VA53LAPNQ Dual component prosthetic hip open approach with combined sources of tissue
  - Other intervention

  Knee replacement:
  - 1VG53LAPNN Dual component prosthetic knee open approach with synthetic material
  - 1VG53LAPNQ Dual component prosthetic knee open approach with combined sources of tissue
  - 1VG53LAPP Tri component prosthetic knee open approach
  - 1VG53LAPPN Tri component prosthetic knee open approach with synthetic material
  - 1VG53LAPPQ Tri component prosthetic knee open approach with combined sources of tissue
  - Other intervention

- **Most responsible diagnosis:** While osteoarthritis makes up the majority of major diagnoses recorded for primary joint replacement, the Expert Panel suggested that patients treated for non-osteoarthritis diagnoses and rare disorders will tend to require different care from typical joint replacement patients, frequently resulting in considerably longer LOS and greater costs. Research supports this hypothesis (45;46).

  Model specification: Dummy variables were included for each of the following ICD-10 diagnosis codes (plus an "other" category) recorded as the MRDx for an observation:

  Hip replacement:
  - M160 Primary coxarthrosis bilateral
  - M161 Other primary coxarthrosis
  - M169 Coxarthrosis unspecified
  - Other diagnosis

Knee replacement:
- M170 Primary gonarthrosis bilateral
- M171 Other primary gonarthrosis
- M179 Gonarthrosis unspecified
- Other diagnosis

- **In/out-of-LHIN residence:** One factor discussed at the Expert Panel was the potential impact that patients requiring travel to a different LHIN for surgery might have on LOS and propensity to be discharged to inpatient rehabilitation.

  Model specification: Dummy variables were included indicating patient residence in the same LHIN as the hospital where surgery was performed or in a different LHIN from the hospital of surgery.
- **Urban vs. rural residence:** Urban vs. rural residence may contribute to differences in terms of the post-acute care and supports that patients receive**.**
  Model specification: Dummy variables indicating patient residence in an area with a Rurality Index of Ontario (RIO) score (52) greater than 40 or a RIO score equal or less than 40

Statistical Methods

Generalized linear regression models were constructed to estimate the significance, direction, and magnitude of influence of the selected patient characteristics on the outcomes of acute inpatient LOS and cost, using negative binomial distribution and a natural log link to account for the skewed distributions of cost and LOS (53). All statistical analyses were performed using SAS (SAS Institute Inc., Cary, NC, US).

Effects coding was used for categorical variables (i.e., values of −1, 1, or 0) rather than dummy coding (i.e., values of 0 or 1). With this approach, the estimated effects for each variable are effects compared to the population mean, rather than a reference group as in dummy coding. Effects coding allows for calculation of percent increase/decrease in the outcome measure for each category, for each predictor variable.

A significance level of 0.05 was used for all statistical analyses. Models were first estimated with all available predictor variables. Then, after identifying the significant predictor variables, the models were re-estimated with only the significant predictors.

The percent change for a given predictor variable was calculated according to the following: Let B represent the parameter estimate for a predictor variable. Then:

$$\% \text{ change} = [\exp(B) - 1] * 100\%$$

The results show the percentage change in an outcome due to the presence of a given category for a given predictor variable. For example, a percentage change of 23.3% in acute LOS for hip replacement patients aged 75 years and older shows that hip replacement patients in that age group have a 23.3% longer acute LOS in comparison with the mean for the entire hip replacement population. These percentage changes should be interpreted in combination with the intercept, which is presented as a baseline value representing the population mean for any given outcome measure.

95% Wald confidence intervals were produced for the parameter estimates and used to calculate the confidence intervals for the percentage changes using the same approach used to calculate the percentage difference.

Results

Results for Primary Hip Replacement

Consistent with similar results found in the primary hip replacement literature, (45) some evidence of a U-shaped association was found between age and cost, with patients aged 49 years and under and 75 years or over having slightly higher acute care costs than those aged between 50 and 74 years (see Table 15 and Figures 9 and 10). This pattern was not evident for acute care LOS, which increased linearly with age. While the associations between all age categories and both of the 2 outcomes were statistically significant, age contributed to much more variation in LOS than variation in cost.

Female patients were found to be associated with slightly longer LOS and very marginally greater costs than male patients. These findings were statistically significant but the very small effect size may not be meaningful.

Although the analysis of MRDx codes showed a trend towards longer LOS with diagnosis of "Primary coxarthrosis bilateral" decreasing with "Other primary coxarthrosis" and further with "Coxarthrosis unspecified," confidence intervals overlapped between the diagnoses and the trend was not consistent for cost, with "Coxarthrosis unspecified" having slightly higher costs than the other 2 diagnoses. While the 3 osteoarthritis diagnoses codes that make up 92% of the total primary hip replacement population (see Table 3) had mixed effects on LOS and cost with a relatively small range of variation between them, the smaller "Other diagnosis" (non-osteoarthritis) category (8% of the total population) was associated with much longer LOS and significantly greater costs (26.9% and 14.7% greater than the population mean, respectively).

Comorbidity was found to have a significant impact on both cost and LOS. Each increasing level of the Comorbidity Index (i.e., 0 Charlson conditions, 1–2 Charlson conditions, and ≥ 3 Charlson conditions) was associated with a substantial increase in both cost and LOS.

The 4 most common types of hip replacement procedures were associated with differences in costs and LOS; for example, "Dual component prosthetic hip open approach with synthetic material" was associated with 6.8% greater acute care costs than the population mean, while "Dual component prosthetic hip open approach" was associated with 5.3% shorter LOS and 5.9% lower costs. However, the confidence intervals for the effects on both outcomes overlapped between several of these procedures. Of note, the small number (less than 3.5%) of "Other intervention" (i.e., not one of the 4 most common procedure codes) cases were associated with a significantly longer LOS but not greater costs.

Patient residence outside of the LHIN of surgery was not found to have a significant impact on LOS but was associated with slightly greater cost. Rural residence was associated with shorter LOS and lower costs than urban residence.

The tiny (approximately 50 annual cases) population of simultaneous bilateral hip replacements had—as expected—far longer LOS and greater costs than the general hip replacement population.

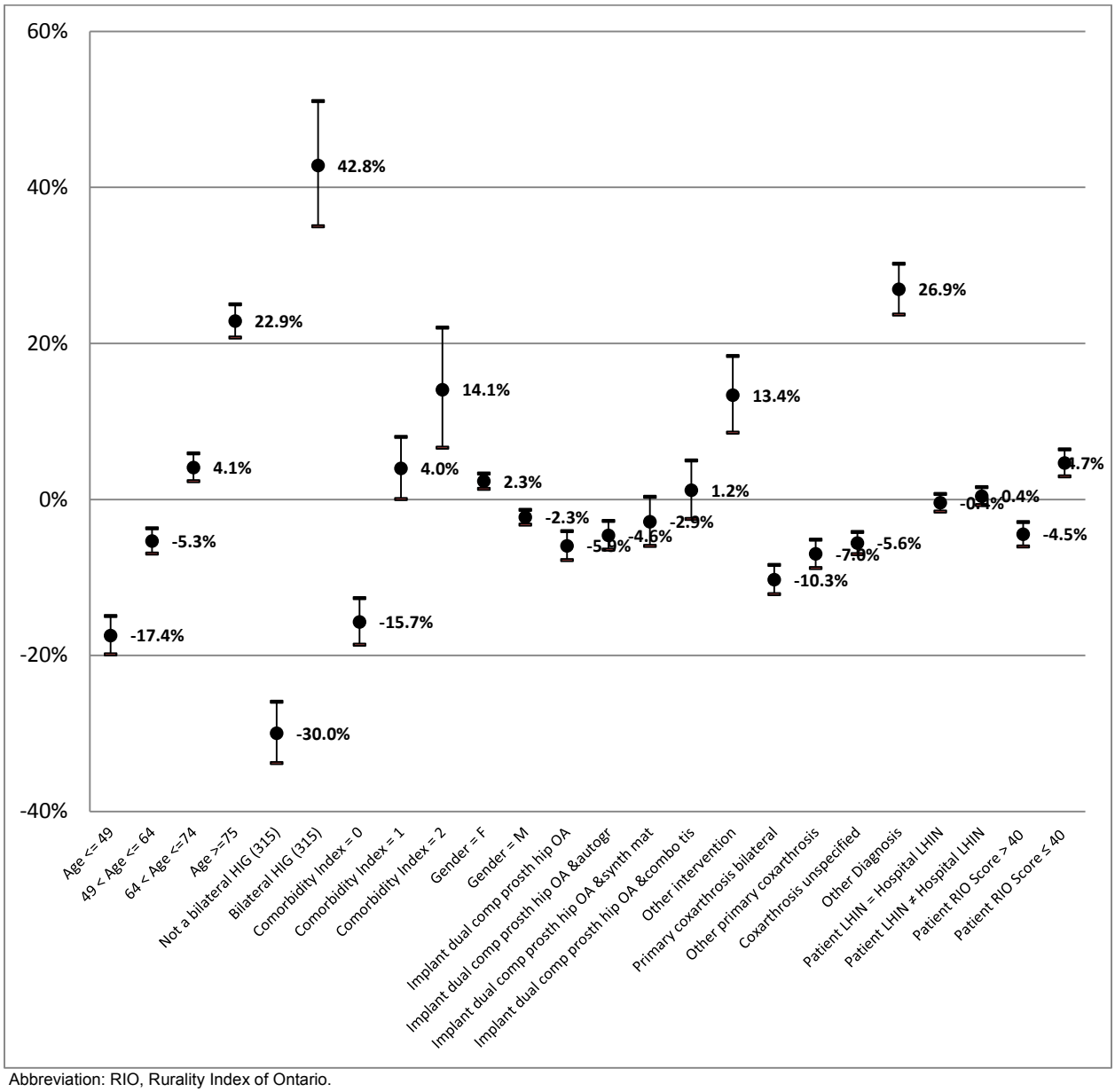
Table 15. Primary Hip Replacement: Estimated Effects of Patient Characteristics on Acute Care Length of Hospital Stay and Acute Care Costs (2011/2012)

		Percent Change (95% CI)	
	Patient Characteristics	**Acute Care LOS**	**Acute Care Costs**
Age, years	≤ 49	−17.4 (−19.9 to –14.9)	2.5 (0.6 to 4.5)
	50–64	−5.3 (–6.9 to –3.7)	−1.2 (−2.4 to –0.1)
	65–74	4.1 (2.3 to 5.9)	−4.1 (−5.3 to –2.9)
	≥ 75	22.9 (20.8 to 25.0)	3.0 (1.7 to 4.4)
Unilateral vs. bilateral	Unilateral	–30 (–33.8 to –25.9)	–30.9 (–34.2 to –27.3)
	Bilateral	42.8 (35.0 to 51.1)	44.6 (37.6 to 52.0)
Comorbidity index[d]	Comorb_index = 0	−15.7 (–18.6 to –12.7)	−11.7 (−14.4 to −8.9)
	Comorb_index = 1	4.0 (0.1 to 8.0)	0.9 (−2.4 to 4.3)
	Comorb_index = 2	14.1 (6.6 to 22.0)	12.2 (5.8 to 19.1)
Sex	Female	2.3 (1.3 to 3.3)	0.9 (0.2 to 1.6)
	Male	–2.3 (–3.2 to –1.3)	–0.9 (–1.6 to –0.2)
Procedure type	1VA53LAPN Dual component prosthetic hip open approach	–5.9 (–7.8 to –4.1)	–5.3 (–6.8 to –3.7)
	1VA53LAPNA Dual component prosthetic hip open approach with autograft	–4.6 (–6.4 to –2.7)	–5.6 (–7.1 to –4.2)
	1VA53LAPNN Dual component prosthetic hip open approach with synthetic material	−2.9 (−6.0 to 0.4)	6.8 (4.2 to 9.4)
	1VA53LAPNQ Dual component prosth. hip open approach w/ comb. sources of tissue	1.2 (−2.5 to 5.0)	3.9 (0.8 to 7.1)
	Other intervention	13.4 (8.6 to 18.4)	0.8 (−2.9 to 4.7)
MRDx	M160 Primary coxarthrosis bilateral	–10.3 (–12.1 to –8.4)	–4.9 (–6.3 to –3.5)
	M161 Other primary coxarthrosis	–7.0 (–8.8 to –5.2)	–5.4 (–6.7 to –4.2)
	M169 Coxarthrosis unspecified	–5.6 (–7.0 to –4.2)	–3.0 (–4.1 to –1.9)
	Other diagnosis	26.9 (23.7 to 30.2)	14.7 (12.4 to 16.9)
LHIN of residence	Same LHIN as hospital	−0.4 (−1.6 to 0.7)	–2.5 (–3.2 to –1.7)
	Different LHIN from hospital	0.4 (−0.7 to 1.7)	2.5 (1.8 to 3.3)
Urban vs. rural	Urban (RIO Score ≤ 40)	4.7 (3.0 to 6.4)	1.8 (0.5 to 3.2)
	Rural (RIO Score > 40)	–4.5 (–6.0 to –2.9)	–1.8 (–3.1 to –0.5)
Intercept		6.17 days (5.70 to 6.67 days)	$17,313 ($16,309 to $18,379)

Abbreviations: CI, confidence interval; RIO, Rurality Index of Ontario).

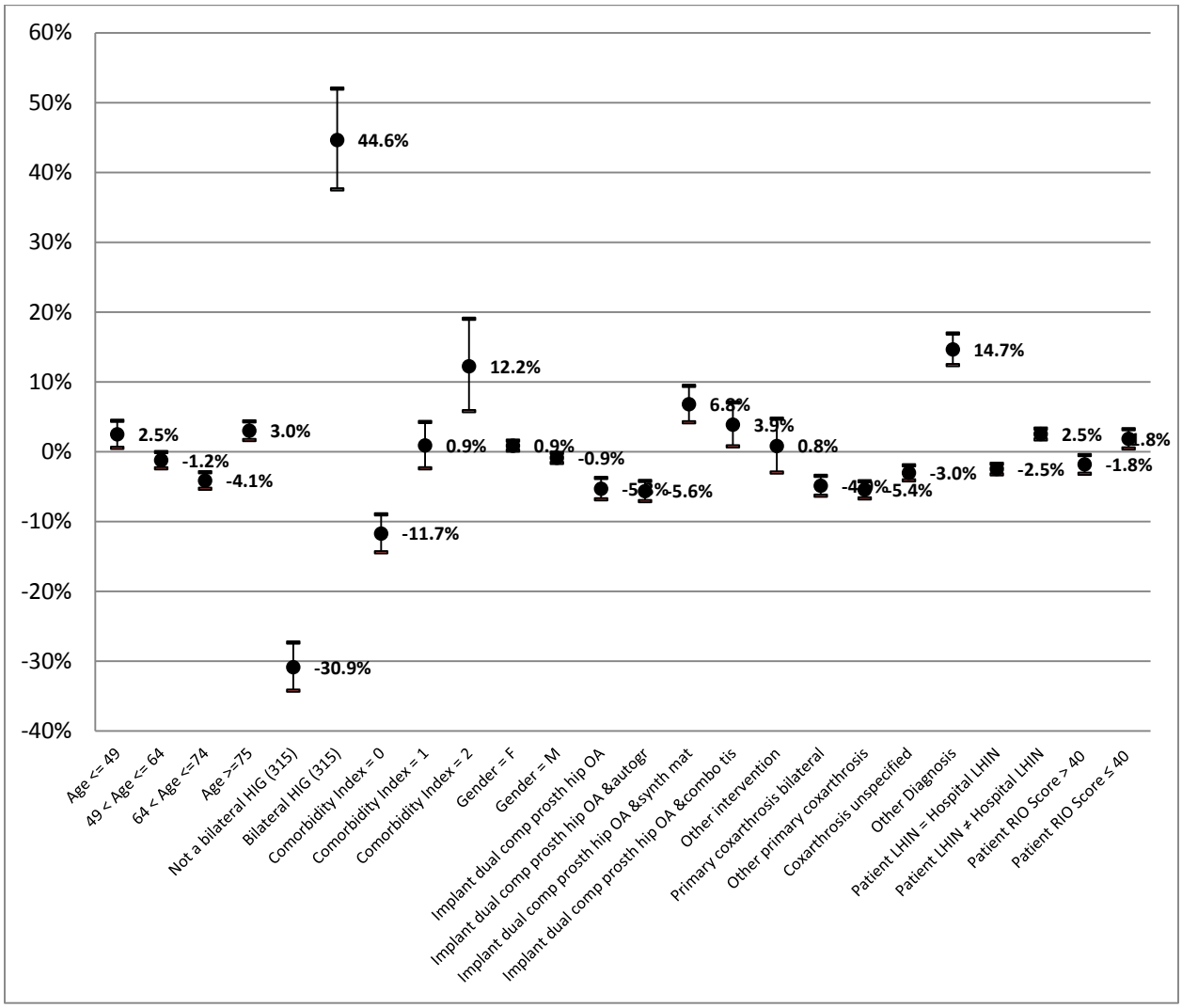
[a]The comorbidity index used in this analysis is defined by Charlson Comorbidity Index score.

Predictive factors analysis prepared by Andrew Tsegelsky, Saad Rais, and Kamil Malikov from the Health Analytics Branch of the Health System Information Management and Investment Division, Ministry of Health and Long-Term Care (2013).



Abbreviation: RIO, Rurality Index of Ontario.

Figure 8. Percent Change in Acute Care Length of Stay Associated With Predictor Variables for Primary Hip Replacement Patients (2011/2012)



Abbreviation: RIO, Rurality Index of Ontario.

Figure 9. Percent Change in Acute Care Cost Associated With Predictor Variables for Primary Hip Replacement Patients (2011/2012)

Results for Primary Knee Replacement

The knee replacement analysis found a very similar pattern of association between age, LOS, and cost as for that for hip replacement: increasing age was associated with longer LOS, with a U-shaped association with cost, where patients aged under 50 and 75 or over had greater costs than the population mean (see Table 16 and Figures 11 and 12).

Different varieties of osteoarthritis diagnosis coded differed in LOS and cost, with "Other primary gonarthrosis" associated with greater LOS and costs than the other 2 categories, "Primary gonarthrosis bilateral" and "Other primary gonarthrosis." As with hip replacement, the non-osteoarthritis "Other diagnosis" category was associated with considerably longer LOS (18.7%) and greater cost (12.7%) than the population average.

As with hip replacement, comorbidity level also had a significant positive relationship with both LOS and cost, with higher levels of comorbidity being associated with considerably greater costs and LOS.

Some significant differences in LOS were observed between different varieties of knee replacement procedure type, with "Tri component prosthetic knee open approach" associated with a LOS 18.7 shorter than the knee replacement population average, but a cost that was not statistically different than the average. Conversely, "Tri component prosthetic knee open approach with synthetic material" and "Tri component prosthetic knee open approach with combined sources of tissue" were both associated with significantly longer LOS but minimal or insignificant differences in costs. The "Other intervention" category was associated with slightly higher costs and LOS.

Out-of-LHIN residence was associated with slightly higher LOS and costs than in-LHIN residence. Similar to hip replacements, rural knee replacement were associated with a shorter LOS but not significantly associated with cost.

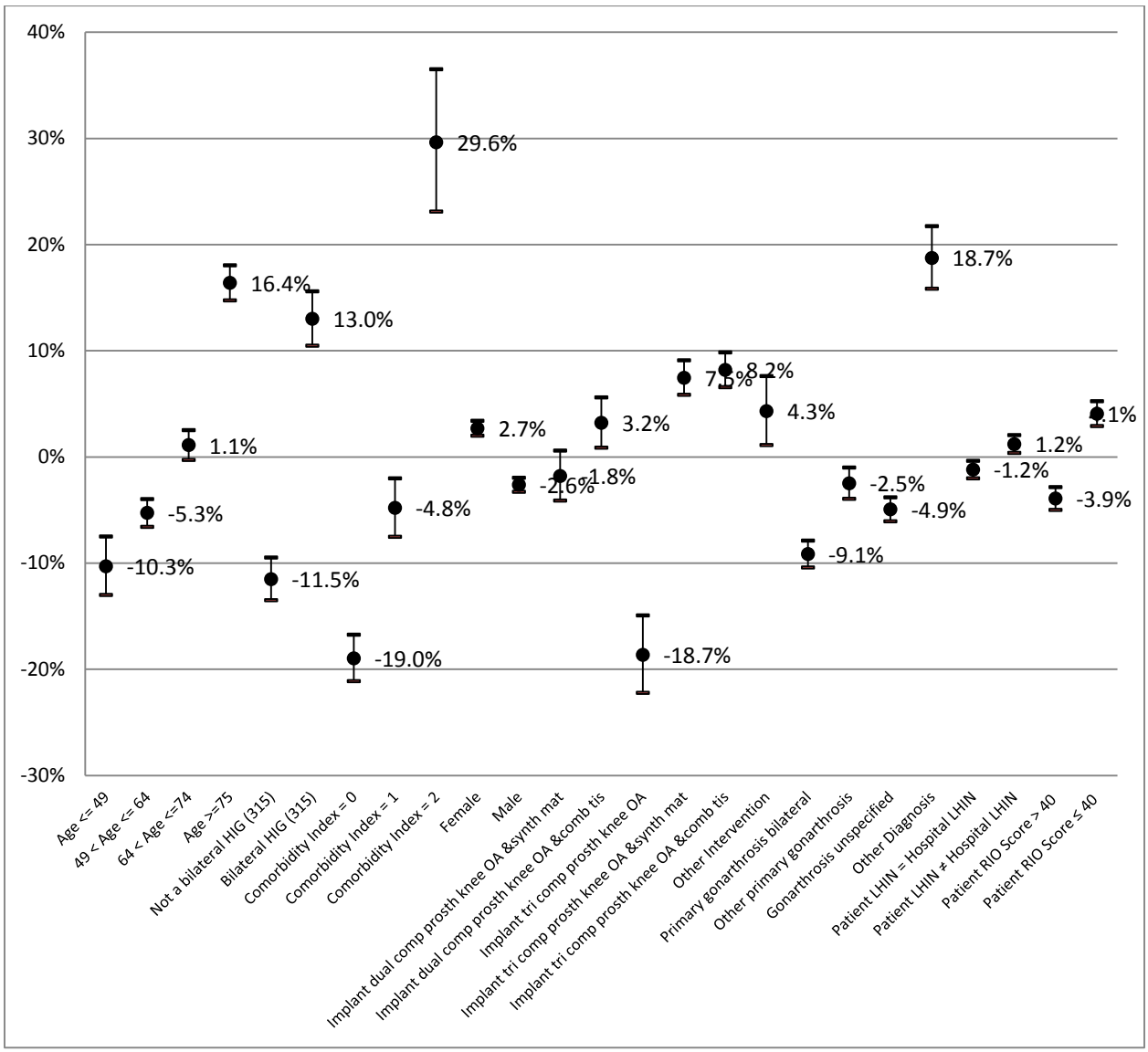
Table 16. Primary Knee Replacement: Estimated Effects of Patient Characteristics on Acute Care Length of Stay and Acute Care Costs (2011/2012)

		Percent Change (95% CI)	
	Patient Characteristics	**Acute Care LOS**	**Acute Care Costs**
Age, years	≤ 49	−10.3 (−13.0 to −7.5)	2.0 (−0.2 to 4.2)
	50–64	−5.3 (−6.6 to −4.0)	−2.2 (−3.2 to −1.2)
	65–74	1.1 (−0.3 to 2.5)	−2.9 (−3.9 to −1.9)
	≥ 75	16.4 (14.8 to 18.1)	3.3 (2.1 to 4.4)
Unilateral vs. bilateral	Unilateral	−11.5 (−13.5 to −9.5)	−17.0 (−18.3 to −15.6)
	Bilateral	13.0 (10.5 to 15.6)	20.4 (18.5 to 22.5)
Comorbidity index[d]	Comorb_index = 0	−19.0 (−21.1 to −16.8)	−17.7 (−19.6 to −15.7)
	Comorb_index = 1	−4.8 (−7.5 to 2.0)	−6.6 (−8.9 to −4.1)
	Comorb_index = 2	29.6 (23.1 to 36.5)	30.0 (24.1 to 36.2)
Sex	Female	2.7 (2.0 to 3.4)	0.2 (−0.3 to 0.8)
	Male	−2.6 (−3.3 to 2.0)	−0.2 (−0.8 to 0.3)
Procedure type	1VG53LAPNN Dual component prosthetic knee open approach with synthetic material	−1.8 (−4.1 to 0.6)	−2.0 (−3.7 to −0.3)
	1VG53LAPNQ Dual comp. pros. knee open approach w/ combined sources of tissue	3.2 (0.9 to 5.6)	3.1 (1.5 to 4.7)
	1VG53LAPP Tri component prosthetic knee open approach	−18.7 (−22.2 to −14.9)	−1.9 (−5.1 to 1.3)
	1VG53LAPPN Tri component prosthetic knee open approach with synthetic material	7.5 (5.9 to 9.1)	−2.0 (−3.2 to −0.8)
	1VG53LAPPQ Tri component pros. knee open approach with comb. sources of tissue	8.2 (6.6 to 9.8)	0.3 (−0.8 to 1.4)
	Other intervention	4.3 (1.1 to 7.6)	2.8 (0.5 to 5.1)
MRDx	M170 Primary gonarthrosis bilateral	−9.1 (−10.4 to −7.9)	−5.2 (−6.2 to −4.2)
	M171 Other primary gonarthrosis	−2.5 (−3.9 to −1.0)	−2.8 (−-3.9 to −1.7)
	M179 Gonarthrosis unspecified	−4.9 (−6.1 to −3.8)	−3.8 (−4.7 to −2.8)
	Other diagnosis	18.7 (15.8 to 21.7)	12.7 (10.4 to 15.1)
LHIN of residence	Same LHIN as hospital	−1.2 (−2.0 to 0.4)	−1.6 (−2.2 to −1.0)
	Different LHIN from hospital	1.2 (0.4 to 2.0)	1.6 (1.0 to 2.2)
Urban vs. rural	Urban (RIO Score ≤ 40)	4.1 (2.9 to 5.3)	0.6 (−0.3 to 1.6)
	Rural (RIO Score > 40)	−3.9 (−5.0 to −2.8)	−0.6 (−1.6 to 0.4)
Intercept		4.18 days (3.99 to 4.39 days)	$13,836 ($12,987 to $13,405)

Abbreviations: CI, confidence interval; RIO, Rurality Index of Ontario.

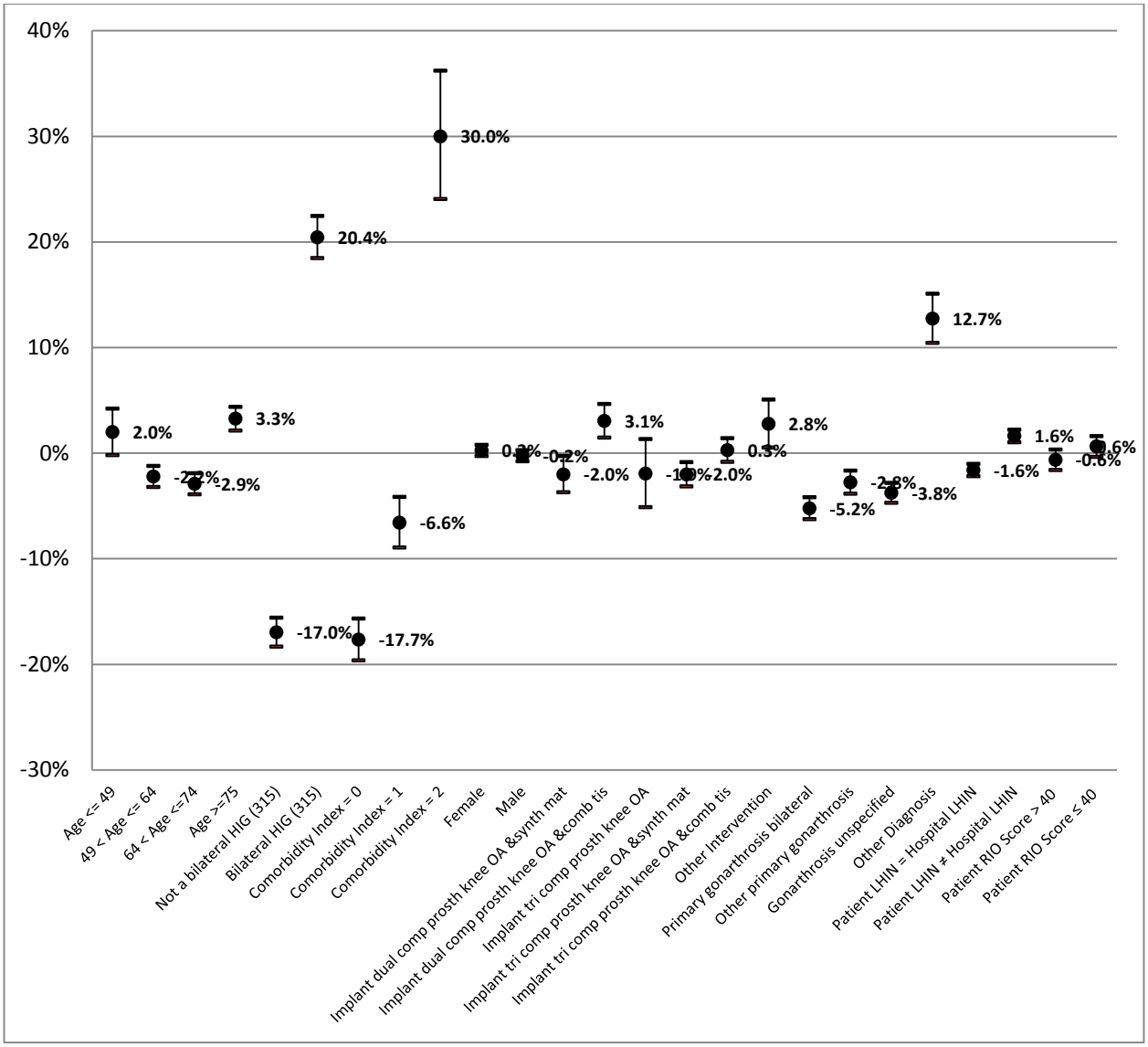
[a]The comorbidity index used in this analysis is defined by Charlson Comorbidity Index score.

Predictive factors analysis prepared by Andrew Tsegelsky, Saad Rais, and Kamil Malikov from the Health Analytics Branch of the Health System Information Management and Investment Division, Ministry of Health and Long-Term Care (2013).



Abbreviation: RIO, Rurality Index of Ontario.

Figure 10. Percent Change in Acute Care Length of Hospital Stay Associated With Predictor Variables for Primary Knee Replacement Patients (2011/2012)



Abbreviation: RIO, Rurality Index of Ontario.

Figure 11. Percent Change in Acute Care Costs Associated With Predictor Variables for Primary Knee Replacement Patients (2011/2012)

Conclusions and Recommendations for Patient Complexity Adjustment Variables

The results of the multivariate analysis demonstrated that the following patient characteristics are most strongly and consistently associated with variation in both acute care length of stay and acute care costs for *both* joint replacement populations, although some characteristics have a relatively greater effect on either hip or knee replacements:

- **Simultaneous bilateral replacement:** Bilateral replacements performed during the same admission were associated with much greater cost and longer LOS than unilateral replacements, consistent with both findings in the literature (47) and the Expert Panel's clinical experience. These effects were even greater for bilateral hip replacements, although they make up a tiny proportion of total cases (fewer than 50 cases each year).
- **Comorbidity level:** Consistent with findings in the literature (35;36;38;45-47) and the Expert Panel's experience, increasing levels of comorbidity were associated with significantly higher costs and longer LOS. These effects were even greater for knee replacements.

It is important to note the difficulties encountered in identifying an administrative data-based definition for comorbidities that resulted in prevalence figures consistent with the Expert Panel's clinical experience. The initial version of this analysis populated the Charlson index with only those conditions coded as a Type 1 Pre-Admit Comorbidity diagnosis. CIHI coding standards require that this diagnosis type only be coded in cases where a comorbid condition has resulted in either 24 hours or more of additional LOS or in the use of additional specialist consultations or interventions. Using this definition, fewer than 1.5% of cases had 1 or more comorbidities recorded; this figure was rejected by the Expert Panel as having no face validity in their clinical experience, where the presence of comorbidity is often the norm rather than the exception.

The analysis was subsequently rerun with the Charlson calculation expanded to include conditions recorded as Type 3 Secondary Diagnosis. Based on CIHI coding standards, these conditions were not seen to have had a sufficient impact on hospital utilization to qualify as Type 1 diagnoses; nonetheless, the results of the analysis clearly show these conditions do have a significant impact on both cost and LOS, although not at the same magnitude as Type 1 diagnoses. Most importantly, this expanded definition resulted in just over 10% of the population having one or more comorbidities recorded (see Table 3). While a vast improvement in face validity over the initial definition, the Expert Panel members still felt this number was considerably smaller than their clinical experience would suggest. Although the Charlson index is a well-accepted comorbidity index that is widely used in health service research, including a number of studies on primary joint replacement, (38;45) and was initially endorsed by Expert Panel members, the index was not initially designed for joint replacement patients and does not capture some of the major comorbidities found in this population such as anemia and atrial fibrillation, which the descriptive analyses in Tables 12 and 13 suggest are both fairly prevalent and associated with increased resource utilization.

- **Non-osteoarthritis Most Responsible Diagnosis:** Most Responsible Diagnosis conditions that differ from osteoarthritis are associated with much higher costs and longer LOS for both hip and knee replacement patients. This finding is consistent with both prior results in the literature

(45;46) and the clinical experience of the Expert Panel, who noted that the joint replacement patients with uncommon diagnoses (approximately 8% of unilateral hips and 3.5% of unilateral knees) tended to require notably different care pathways and additional interventions in comparison to typical osteoarthritis patients.

- **Age:** Increasing age is associated with longer LOS for both primary hip and knee replacement. Age has a 'U-shaped' effect on costs, with relatively young and relatively old patients having higher costs than the population mean.

  The Expert Panel noted that the increased costs observed in relatively young patients were likely due to the use of more expensive varieties of prostheses in younger patients with longer life expectancies and higher activity levels.

  Panel members also commented that age may not be an independent risk factor in itself, but may instead be a proxy for greater severity and further progression of underlying disease.

While other characteristics demonstrated various significant associations with LOS and cost in some of the individual models, the factors above were considered to have the most consistent impacts on both acute care LOS and costs in both hip and knee replacement models. Hence, it is recommended that the factors above be incorporated into clinical or policy applications focused on the primary joint replacement pathway, including the following:

- **Care pathways and guidelines** should include consideration of patients' age and comorbidities (either in terms of specific comorbidities or overall comorbidity burden) as they relate to variation in the types and quantities of interventions required; for example, patients with cardiac comorbidities may require additional diagnostic interventions. Patients with non-osteoarthritis primary diagnoses may require a different pathway of care from routine osteoarthritis joint replacement pathways.
- **Funding methodologies** (such as the Quality-Based Procedures [QBPs]) need to include risk adjustment or risk stratification the key patient characteristics described above in order to fairly compensate providers for variation in patient complexity. The Expert Panel has recommended that simultaneous bilateral replacements be funded as a separate group. Within each of the 3 recommended patient groups, the current HIG acute inpatient grouping and weighting methodologies should incorporate variables for the patient characteristics described above. The Health-Based Allocation Model Inpatient Grouper methodology currently includes some consideration of different patient age groups; these age variables should be aligned with the results of the analysis presented here. Similarly, CIHI's Case Mix Groups+ (CMG+) methodology includes consideration of comorbidity severity level for some groups; the QBP methodology should include a similar comorbidity adjustment within each of the 3 patient groups. Finally, a funding adjustment should be made for non-osteoarthritis MRDx, which evidence shows to result in a different pathway of care than for routine joint replacement.
- **Performance measurement systems** (such as the QBP Integrated Scorecard) should either stratify or exclude simultaneous bilateral replacements from measurement of the broader joint replacement population. Indicators (or their targets / benchmarks) should be risk adjusted for patients' age and comorbidity level. Cases with non-osteoarthritis MRDx should either be excluded, stratified separately for measurement or subject to additional risk adjustment.

Limitations and Recommendations for Future Analysis

This analysis was limited by the time, resources, and data available during the course of Health Qualtity Ontario's (HQO) project work with the Expert Panel. The range of outcomes analyzed is limited: while acute care costs and LOS are likely to provide a reasonably good proxy for overall utilization, future analyses should also measure outcomes across other care settings included in the episode of care; prior studies in Ontario have demonstrated that this is feasible through linking datasets and provides a more comprehensive picture of costs, utilization and outcomes across the full continuum of care (24;43). Such analyses will be critical for supporting future shifts towards more integrated, "bundled" payment and performance measurement mechanisms spanning multiple providers.

An outcome recommended for future analysis is patients' propensity for discharge to an inpatient rehabilitation setting (compared with discharge home). While nearly all LHINs have now shifted to discharging 90% or more of their joint replacement patients home, the Expert Panel felt that a certain proportion of patients will always continue to require the additional level of care provided in an inpatient rehabilitation setting, due to medical or social complexity Achieving a better understanding of the characteristics of patients currently being discharged to inpatient rehabilitation would help to inform recommendations around eligibility and appropriateness criteria for these settings.

This analysis may benefit from use of alternate methodological approaches. For instance, the effects coding approach for variables used in this analysis (as in HQO's previous Hip Fracture project) enables estimates to be made of the effect of each independent variable against the mean outcome for the overall hip or knee replacement population. This approach may be cumbersome in cases where a variable of interest is found in a relatively small number of observations or should be interpreted against a larger reference category. For instance, it is more intuitive to interpret the incremental effects on cost and LOS of simultaneous bilateral replacements against a (much larger) reference group of unilateral replacements, rather than the mean values of a population containing both groups.

The approach towards capturing comorbidities in this is incomplete and it is strongly recommended that future analyses be conducted employing alternate approaches. While widely used in health services research, the Charlson index captures a relatively limited range of diseases and does not include some key conditions such as sleep apnea, anemia and atrial fibrillation that were identified as important by the Expert Panel and that descriptive analysis shows are found in relatively large numbers in this population and appear to be associated with increased costs and LOS (see Tables 13 and 14). In the United States, the Centres for Medicare & Medicaid Services (CMS) has developed publicly reported performance indicators for readmission and complication rates following total joint replacement that may provide some useful methodological lessons for Ontario: these measures employ comprehensive risk adjustment models that include nearly 30 different comorbidities, some of which—such as morbid obesity and protein-calorie malnutrition—were estimated to have greater odds ratios than most of conditions included in the traditional Charlson index (54;55). Future Ontario analyses should employ a more comprehensive set of comorbidities that is more clinically meaningful to the joint replacement population. The Expert Panel also suggested that a standardized questionnaire could be piloted to prospectively collect this data.

Finally, the scientific literature and the Expert Panel identified a number of patient characteristics that are not currently captured in provincial hospital administrative data, but may nevertheless be important determinants of variations in care. These include medical characteristics such as patients' ASA score and social factors such as patients' marital status and caregiver supports. Much of this information is currently captured in some form or another during the pre-surgical phases of the pathway, such as assessments

conducted in coordinated intake centres and pre-admit screening clinics. Collecting this information at the provincial level would be of great value for policy.

Primary Hip and Knee Replacement Episode of Care Model

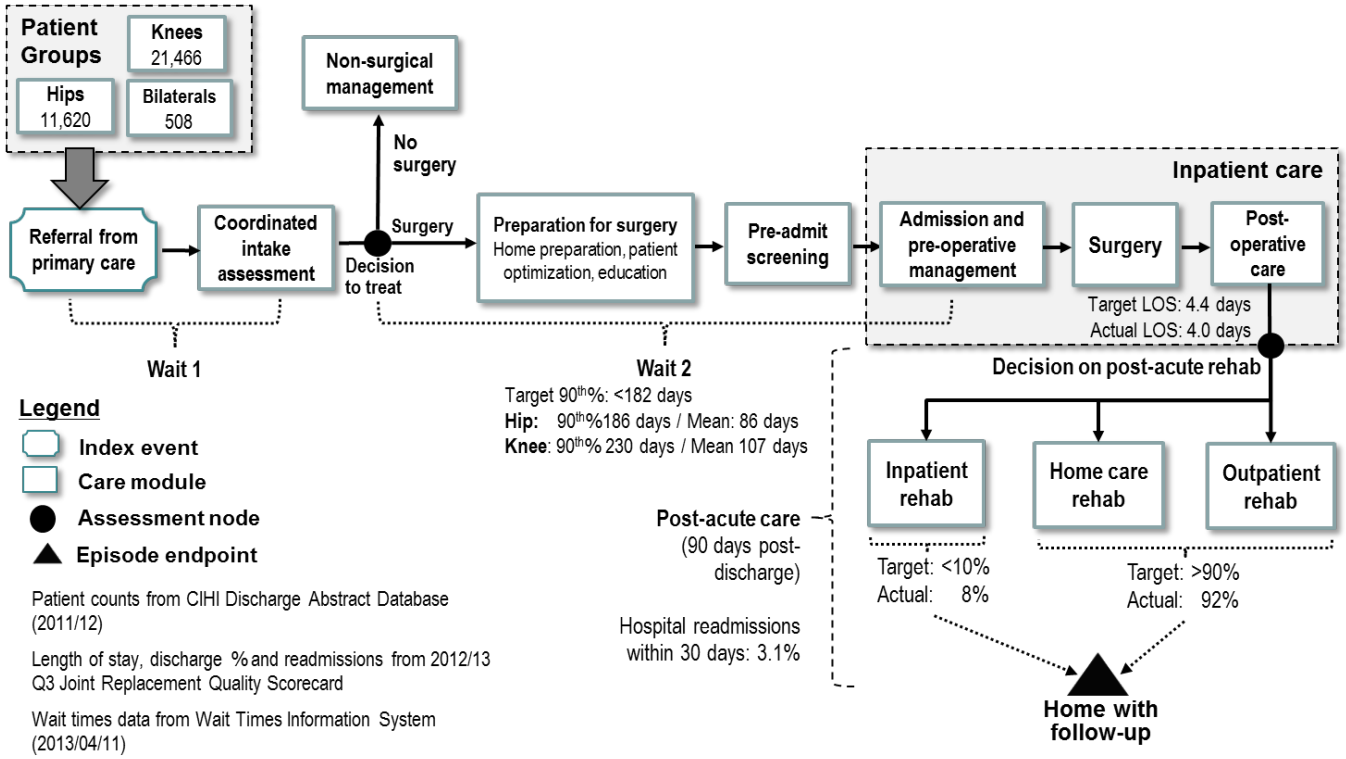


Figure 11: Episode of Care Model for Primary Hip and Knee Replacement

Recommended Practices for Primary Hip and Knee Replacement

Evidence Sources and Guidelines Identified

OHTAC Recommendations

Three HQO evidence-based analyses and corresponding OHTAC recommendations were identified that directly related to the hip and knee replacement episode of care:

- Metal-on-Metal Hip Resurfacing Arthroplasty: An Analysis of Safety and Revision Rates (56)
- Physiotherapy Rehabilitation After Total Knee or Hip Replacement: An Evidence-Based Analysis (57)
- Technologies for Osteoarthritis of the Knee: An Evidence-Based Analysis (58)

HQO Rapid Reviews

Rapid reviews were conducted on specific topics where gaps or inconsistencies in the evidence were identified or as requested by the Expert Panel:

- Anaesthesia Among Patients Undergoing Knee Arthroplasty: A Rapid Review
- Local Infiltration Analgesia in Hip and Knee Arthroplasty: A Rapid Review
- Antibiotic-Laden Bone Cement for Primary Knee Arthroplasty: A Rapid Review
- The Effectiveness of Cement in Primary Hip Replacements: A Rapid Review
- Simultaneous or Staged Bilateral Knee Arthroplasty: A Rapid Review
- Intensity of Rehabilitation During the Acute Hospitalization Period After Hip or Knee Arthroplasty: A Rapid Review

Complete rapid review reports are available in Appendix I. The conclusions of the reviews are included within each of the modules.

As stated by the GRADE Working Group (59), the final GRADE quality score (59) can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Clinical Guidelines

The guideline review process identified 1 Canadian guideline that was used as the reference standard due to its relevance and local context:

- **Bone and Joint Canada**: Bone and Joint Canada Hip and Knee Replacement Surgery Toolkit (2009) (19)
  - A supplementary literature review was conducted in support of the Bone and Joint Canada Toolkit. (60) Key findings identified from the literature review were referenced during the development of the recommended practices for the Hip and Knee Episode of Care.

Four additional international clinical guidelines encompassing the entire hip and/or knee replacement episode of care were identified:

- **NSW**: New South Wales Agency for Clinical Innovation. Evidence Review on Preoperative, Perioperative and Postoperative Care of Elective Primary Total Hip and Knee Replacement (2012) and the corresponding publication by Mak et al (2013) (17;61)
- **Dutch**: Dutch Guideline on Total Hip Prosthesis (2011) (62)
- **BOA**: British Orthopaedic Association. Primary Total Hip Replacement: A Guide to Good Practice (2012) (7)
- **BOA**: British Orthopaedic Association. Knee Replacement: A Guide to Good Practice (1999) (8)

Quality assessment using the AGREE domain scores for each of the guidelines are presented in Table 17. Given the limited number of guidelines identified for each cohort, all guideline recommendations were included for consideration by the Expert Panel.

Table 17. AGREE II Domain Scores for Hip and Knee Replacement Guidelines

Guideline, Year	AGREE II Domain (*maximum possible score*)					
	Scope & Purpose *(out of 21)*	**Stakeholder Involvement** *(out of 21)*	**Rigour of Development** *(out of 56)*	**Clarity of Presentation** *(out of 21)*	**Applicability** *(out of 28)*	**Editorial Independence** *(out of 14)*
Bone & Joint Canada, 2009 (19)	13	12	23	9	17	4
NSW, 2013 (17)	18	11	31	15	6	6
Dutch, 2011 (62)	6	4	25	14	5	5
BOA Hip, 2012 (7)	10	9	13	9	5	2
BOA Knee, 1999 (8)	10	8	13	8	6	2

The guidelines supporting HQO Expert Panel recommendations, along with quality of evience and quality assessment tools, are summarized in Table 18.

Table 18. Summary of Evidence Assessments Used by Included Guidelines

Bone and Joint Canada, 2009 *Supplementary Review*[a]	NSW, 2013	Dutch, 2011	BOA Hip, 2012	BOA Knee, 1999
Suggestive Evidence: ≥ 1 RCTs rated as good or excellent; ≥ 1 SR rated good or excellent **Emerging / Inconclusive Evidence**: ≥ 1 RCTs rated as fair; ≥ 1 SR rated fair; ≥ 1 other type of research rated fair or above	**Grade of Evidence:** Body of evidence can/is **A:** trusted to guide practice **B**: trusted to guide practice in most situations **C**: provides some support for recommendation(s) but care should be taken in application **D**: weak and recommendation must be applied with caution	**Level of Evidence:** **A1:** SR/MA of ≥ 2 independently conducted studies of **A2** level **A2: Interventional Studies:** RCTs of good quality **A2: Harm, Side Effects, Etiology, Prognosis Studies:** prospective cohorts of good quality **B: Interventional Studies:** clinical trial of poor quality or inadequate number of participants (including case-control, cohort study) **B: Harm, Side Effects, Etiology, Prognosis Studies:** prospective cohort of poor quality or retrospective cohort or case-control study **C:** non-comparative study **D:** expert opinion	No systematic evidence base provided[b]	No systematic evidence base provided[b]

Abbreviations: BOA, British Othropaedic Association; MA, meta-analysis; NSW, New South Wales SR, systematic review
[a]The evidence assessment presented is based on the supplementary literature review referenced by the Bone and Joint Canada Toolkit. (60) All recommendations from the Bone and Joint Canada Toolkit that were beyond the scope of the key findings summary table of this supplementary literature review were considered to be based on Expert Opinion.
[b]No systematic literature review was conducted. While some recommendations have individual references noted, due to the nature of how the BOA recommendations were formed they are considered to be based on Expert Opinion.

Other Relevant Resources

Three additional resources identified by the Expert Panel that were considered important to specific components of the hip and knee replacement episode of care were also referenced:

- National Institute for Clinical Excellence. Guidance on the Selection of Prostheses for Primary Total Hip Replacement (2000) (63)
- American College of CHEST Physicians Evidence-Based Clinical Practice Guidelines. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed (2012) (64)
- Institute for Healthcare Improvement. Enhanced Surgical Site Infection Prevention Bundle: Hip and Knee Arthroplasty How-to Guide (2011) (65)

Episode of Care Recommended Practices

Several recommendations within the episode of care pathway refer to events that can begin or end in different modules. Modules should be considered collectively rather than as individual components. Individual health care networks should work to minimize duplication of tests and efforts.

Module 1: Referral from Primary Care

Upon review of technologies for osteoarthritis of the knee (66), OHTAC recommended that:

- Total knee replacement be recommended as an appropriate treatment for osteoarthritis of the knee for patients with progressive disease despite the use of optimal drug therapy.
- Access to total knee replacement be improved by the more efficient utilization of orthopedic surgical time, public education to better inform individuals about the benefits of total knee replacement, clinical practice guidelines to guide physicians on the eligibility criteria for total knee replacement, appropriate primary care for these patients, and criteria for appropriate referrals to orthopedic surgeons

This module identifies recommended practices for the early assessment and referral of patients for hip or knee replacement within the primary care setting.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
Diagnostics and Radiographs	
1.1 The referring practitioner should provide standard radiograph investigations of the affected joints. Knee Radiographs: • Anterior-posterior, weight bearing of both knees • Skyline views of the affected knee(s) at 30 degrees • Lateral views of the affected knee(s) (if possible standing) Additional radiographs may be ordered by the surgeon as part of pre-surgical planning Hip Radiographs: • Anterior-posterior pelvis centered at pubis to show proximal one third of both femurs • Shoot through lateral aspect of affected hip and proximal femur Additional radiographs may be ordered by the surgeon as part of pre-surgical planning.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
1.2 Pre-consultation MRIs are rarely indicated and should not be routinely ordered.	Based on Expert Panel consensus.
Process for Referral	
1.3 The primary care provider (PCP) should make the referral for surgery consultation and be the coordinator of patient care.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel; agrees with the BOA (*Expert Opinion*). (7)

1.4 Self-referral should be considered for patients who do not have a PCP.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
1.5 Referrals should be made through a standardized template that includes the reason for referral, radiographs of the affected joint(s), and relevant patient comorbidities.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.

Module 1: Implementation Considerations

Barriers	• Currently there is no standardized provincial joint replacement referral protocol or Electronic Health Record (EHR) to support it. • Many primary care providers are not aware of what constitutes a quality referral package. • While some hospitals and LHINs have their own standard joint replacement referral templates, even PCPs who have access to these do not always use them; many PCPs choose to "scribble referrals on a napkin" – orthopedic surgeons will still accept these as they do not wish to turn away referred cases • Many PCPs provide inappropriate / low quality radiographs with referrals, requiring repeat x-ray procedures – e.g., orthopedic surgeons often receive x-rays with patients in a non-weight bearing position. • Many PCPs continue to perform unnecessary MRIs of affected joints, which are nearly always useless; anecdotally, these inappropriate diagnostics are often ordered to "buy time" for the patient to recover from their complaint naturally.
Potential Levers	• Develop evidence-based provincial standards for appropriate patient work-up, including appropriate diagnostic imaging guidelines, and disseminate through Ontario College of Family Physicians, Association of Family Health Teams of Ontario, and through feedback to family physicians by orthopedic surgeons and (preferably) coordinated intake centres. • Coordinated intake centres and orthopedic surgeons should return referrals with inappropriate diagnostics to PCPs. To be successful, this strategy will require all professionals performing orthopedic consultations to refuse these referrals, or else a PCP may simply refer somewhere else. • Knowledge Transfer Exchange (KTE) through the Ontario College of Family Physicians regarding referral for assessment and post operative care should be considered.

Module 2: Coordinated Intake and Assessment

This module describes the recommendations related to coordinated intake and assessment of patients referred from primary care. There are a number of different successful models and structures of coordinated intake programs, with the intent of improving patient access to the healthcare system.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
2.1 Hip and knee referrals should be managed through a coordinated intake and assessment process. • The process should be flexible and allow PCPs or patients to refer to a specific surgeon or hospital, or to the next available surgeon or hospital. Patients should be given the option to be referred to another surgeon (or intake) with a shorter waiting time when there are differences across the system. • Patients should be seen within the provincial wait time target; however, they should be allowed to wait beyond the wait-time target for a particular hospital or surgeon if they choose to. • There are multiple models and structures of coordinated intake assessment processes. Hospitals and local healthcare centers should be allowed to select their preferred method of coordinated intake so long as the criteria listed above are satisfied.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
2.2 Patient assessments should be completed by an appropriate health care practitioner qualified and trained to assess patients and to make decisions regarding the appropriateness of surgeon consultation or surgery. • Assessments should include an evaluation of patient history and comorbidities.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
2.3 Every patient scheduled to undergo joint replacement should receive a functional assessment.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.

Module 2: Implementation Considerations

Barriers	• Only a few LHINs have coordinated intakes in place and, where they do exist, there is significant variation not only in their processes and effectiveness, but even in the percentage of hip and knee referrals captured by the coordinated intake. • Measure wait from referral to assessment in a coordinated assessment centre. • Measure wait time from referral to assessment in surgeons office. • For central intake to be effective, orthopedic surgeons and hospitals in a region need to agree to submit all referrals they receive to the coordinated intake. Many orthopedic surgeons in regions with coordinated intakes are still accepting referrals and circumventing the process. • With varying access to a coordinated intake process, family physicians have

	difficulty ensuring quick access to surgery by identifying the next available surgeon and/or hospital.
Potential Levers	• Coordinated intakes already exist in a number of areas, and were funded in 5 LHINs by the Ministry. • 2011 Deloitte evaluation of central intake and assessment centres in Ontario found the model was effective in improving access, efficiency, and other outcomes, but that effectiveness was much higher in those centres that were more mature in their implementation – e.g., captured a greater percentage of local referrals and made more use of allied health professionals for screening referrals before they reached orthopedic surgeons (in some centres, all referrals received a consultation with an orthopedic surgeon regardless ofpre-assessment). ○ http://www.southeastlhin.on.ca/uploadedFiles/Public_Community/Health_Service_Providers/CIAC%20Hip%20and%20Knee%20Final%20Report.pdf • A coordinated intake process should have consistent (provincial?) standards for assessment; e.g., standard investigations and measures. • While it is difficult to implement a provincial directive that all patients be referred to a coordinated intake centre, the Ministry can drive adoption by setting standards; e.g., require that all patients receive referral to next available surgeon/hospital. • The coordinated intake process should provide a triage/severity assessment and ensure timely access to a surgeon based on severity score. • Once standards for primary care work-up and referral are in place, the coordinated intake staff should provide feedback on patient work-up to family physicians with a view to improving service. • Coordinated intake services should meet regularly to reduce variation in wait times across the province. • A standard measurement scale for preoperative functions can be developed and used in the province; e.g., Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). This will also support considerations around appropriateness of surgery.

Module 3: Decision to Treat Clinical Assessment Node

This module represents the clinical assessment node whereby the final decision as to whether a patient receives surgical or non-surgical management occurs. While the decision to undergo non-surgical management is included within the module, the specific care pathway for non-surgical management is beyond the scope of the current episode of care model.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
Surgical Management	
3.1 Surgical patients need to be assessed by a surgeon to make the final decision regarding appropriateness for surgery.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel; agrees with the BOA (*Expert Opinion*). (7;8)
3.2 The risks and benefits of surgery should be explained to the patient, and the patient should be charged with the decision whether or not to proceed with surgery.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel; agrees with the BOA (*Expert Opinion*). (7;8)
Non-Surgical Management	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
3.3 If it is determined that surgery is not appropriate for a patient, the coordinated intake should provide "outbound" care back to the appropriate health care practitioner. • The coordinated intake should provide an appropriate care plan for the management of non-surgical patients, which should include patient education as well as physician instructions such as criteria for return to the intake system.	
3.4 The coordinated intake process should ensure that non-surgical options are explained to the patient.	Based on Expert Panel consensus.
3.5 Results of the assessment and plan for treatment should be communicated back to the patient's PCP.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel; agrees with the BOA (*Expert Opinion*). (8)

Module 3: Implementation Considerations

Potential Levers	• Appropriateness of surgery can be supported by implementing standard measures of pre- and post-operative functional status (e.g., WOMAC), and comparing surgeons and hospitals across these measures. • Prior to referral to surgeon, physiotherapy and nursing assessment should take place. With new funding announcement that provides for physiotherapy services in family health teams, is this an opportunity to drive early assessment? • Standards and protocols need to be developed for non-surgical management. Support needs to be provided to primary care providers for management of non-surgical candidates.

	• Explore use of Sport and Exercise primary care physicians to explore non-surgical options of care. • Family physicians should receive feedback on why patient is not appropriate for surgery with a view to educating family physician on early assessment. • Patient education should follow a standard process where patients are informed on all appropriate treatment options, including both conservative management and surgical treatments.

Module 4: Preparation for Surgery

This module discusses the events that may occur in preparation for hip or knee replacement surgery. Preparation for surgery includes patient education and lifestyle or behaviour modification, as well as provisional discharge planning. This should be done by the appropriate health care provider inside or outside the coordinated intake process.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
4.1 Preparation for surgery should occur with adequate time before surgery to address modifiable patient risk factors.	Based on Expert Panel consensus.
4.2 Patients should receive education addressing the entire continuum of care.	Based on Bone and Joint Canada (*Suggestive Evidence*) (19) and modified by the Expert Panel; agrees with BOA (*Expert Opinion).* (8)
4.3 Discharge planning should begin at the time of the decision to treat. • The patient's home should be prepared for their safe return and recovery after acute care or rehabilitation. • Availability of support persons to assist the patient before and after surgery should be determined.	Based on Bone and Joint Canada (*Suggestive Evidence*) (19) and modified by the Expert Panel; agrees with BOA (*Expert Opinion). (7;8)*
Lifestyle and Behaviour Modification	
4.4 Lifestyle or behaviour modification may be necessary before surgery to optimize the benefit and reduce the risks of surgery.	Agrees with Bone and Joint Canada (*Expert Opinion)* (19) and the NSW *(Grade B*). (17)
4.5 Smoking cessation counselling prior to surgery should be recommended for people who smoke.	Agrees with Bone and Joint Canada (*Expert Opinion)* (19) and the NSW *(Grade B*). (17)
4.6 Weight loss counselling prior to surgery should be recommended for obese and morbidly obese people.	Agrees with Bone and Joint Canada (*Expert Opinion)* (19) and the NSW *(Grade C*). (17)
4.7 Exercise should be recommended, as tolerated, in preparation for hospital admission if indicated by lifestyle risk factors.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
4.8 The following OHTAC recommendation should be considered on preoperative physiotherapy exercise: • The full benefit of a preoperative exercise program for hip and knee replacement is not yet realized	Based on 2005 HQO evidence-based analysis and OHTAC recommendation *(GRADE: moderate). (67)*
Based on the Expert Panel's awareness of evidence published since the OHTAC recommendation, the Expert Panel recommends that OHTAC update the evidence-based analysis and OHTAC recommendation on preoperative exercise.	Request for update to 4.8 based on Expert Panel consensus.

Module 4: Implementation Considerations

Barriers	• Currently, there is no standardized provincial preoperative functional assessment. • While many hospitals now have routine clinical pathways, they are not all consistently developed, with gaps in the evidence and uneven rigour behind the pathways. • Clinical pathways should also be provided to patients to educate them on what to expect; pre-operative patient education materials vary throughout the province.
Potential Levers	• Align hospital clinical pathways to evidence-based recommendations and standards in the Clinical Handbook. • Consider speaking to Accreditation Canada about creating a requirement for accreditation that hospitals have a clinical pathway in place that includes the Clinical Handbook standards. • Develop provincial standards that hospitals are to include in preoperative assessments. • Develop key elements that are to be included in all hospitals' patient education materials. • Hospitals should adopt the new health transformation discharge planning standards in order to meet the provincial target of 4.4-day LOS • All hospitals should have an orthopedic surgery safety check list • Primary care providers should tap into publically funded behavioural modification programs.

Module 5: Pre-Admission Screening

This module describes the recommended practices for screening and assessment of patients before hospital admission with the aim of ensuring safe medical preparation for surgery. Screenings should be standardized to avoid unnecessary or duplication of tests.

Note: At the time of writing of this handbook, HQO was undergoing an evaluation of pre-operative assessment clinics and routine cardiac preoperative tests. The results of these analyses may impact the best practices for the following recommendations.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
Process	
5.1 Pre-admission screenings should be conducted in an appropriate time frame before surgery to avoid empty operating room time due to late cancellations.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
5.2 A multi-disciplinary team is necessary to optimize patient preparation for surgery.	Agrees with Bone & Joint Canada *(Expert Opinion),* (19) the NSW (*Grade B), (17)* and BOA *(Expert Opinion).* (7;8)
5.3 Patients should be medically optimized before elective surgery.	Based on Bone and Joint Canada (*Suggestive Evidence*) (19) and modified by the Expert Panel.
5.4 Specific investigations for medical preparation need to follow evidence-based best practices.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
Blood Management	
5.5 A multidisciplinary blood management program adaptable to individualized patient needs should be implemented. • Available resources should be used to reduce the risk of blood transfusion. • Both pre-operative and operative blood management modalities can be used.	Agrees with Bone and Joint Canada (*Suggestive Evidence)* (19) and the NSW (*Grade B).* (17)
5.6 The Hip and Knee Expert Panel suggest the use of tranexamic acid for prevention of blood loss. Because the use of tranexamic acid is off-label, the decision should rest with the Pharmacy and Therapeutics committee of the hospital.	Based on Expert Panel consensus.

Module 5: Implementation Considerations

Potential Levers	• Pre-operative screening and diagnostics should align with provincial standards of appropriateness (HQO panel on preoperative diagnostics).

Module 6: Admission and Preoperative Management

This module refers to the preoperative management and preparation of patients after hospital admission for their hip or knee replacement surgery.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
6.1 Hospitals should use a structured clinical care pathway. • Care maps should be used with clinical judgement as adjustment may be required for a subset of the population that is unable to meet criteria due to comorbidities or postoperative adverse events.	Based on Bone and Joint Canada (*Expert Opinion)* (19) and modified by the Expert Panel; agrees with NSW (*Grade A)* (17) and the BOA *(Expert Opinion)*. (7)

Module 6: Implementation Considerations

Barriers	• Not all hospitals have clinical pathways that can be used as a basis to inform patients on what to expect while in surgery and post surgery. At a minimum, preoperative management should focus on patient education and planning for the elective procedure.
Potential Levers	• All hospitals should have developed, documented clinical pathways that comply with Accreditation Canada requirements.

Module 7: Surgery

This module describes recommended practices for primary hip and knee replacement surgery. The recommendations are focused on the appropriate selection of anesthesia, analgesia, and surgical implants.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
Surgical Safety	
7.1 The World Health Organization (WHO) surgical safety checklist, in addition to other surgical safety tools and supports, should be referenced prior to surgery. • The checklist is available at: http://www.who.int/patientsafety/safesurgery/ss_checklist/en.	Based on Bone and Joint Canada (*Expert Opinion)* (19) and modified by the Expert Panel; agrees with the BOA *(Expert Opinion).* (7)
Anesthesia	
7.2 The choice of anesthesia should involve the anesthesiologist and surgeon, as well as patient preference.	Agrees with the NSW (*Grade B) (17)* and the BOA *(expert opinion). (7)*
7.3 Neuraxial anesthesia is recommended when appropriate.	For THA: Based on Expert Panel Consensus; agrees with Dutch Guideline (*levels 1 and 2*) (62) and the BOA *(Expert Opinion).* (7) For TKA: **HQO Rapid Review** Regional anesthesia compared to general anesthesia for TKA (see Rapid Review No. 1 in Appendix I): - No significant difference in 60-day mortality *(GRADE: very low)* - No significant difference in hospital length-of stay *(GRADE: very low)* *From an addendum to the Rapid Review examining observational studies:* - Significant decrease in 30-day mortality *(GRADE: low)* - No significant difference in hospital length-of-stay *(GRADE: low)*
Prosthesis Selection	
7.4 Individual hospitals should develop and implement an implant matching program, where appropriate prostheses are determined based on best available, current evidence applied to individual patient characteristics.	Based on Expert Panel consensus.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
7.5 Evidence of clinical effectiveness should be held to national and international standards. • The benchmark set by the National Institute for Clinical Excellence (NICE) for primary total hip arthroplasty prosthesis selection is a revision rate of 10% or less at 10 years. (63) • Prosthesis selection should also take into consideration patient characteristics, surgeon recommendations, cost effectiveness, and the ability to maximize early rehabilitation potential. (63)	Based on Expert Panel consensus, with acknowledgement of the NICE guidance on prosthesis selection for hip replacements. (63)
7.6 If metal-on-metal (MOM) hip resurfacing arthroplasty (HRA) is to be used, the following OHTAC recommendation should be adhered to: • Metal-on-metal HRA is a reasonable treatment option for osteoarthritis patients who meet appropriate criteria. o Expert opinion informed that the appropriate criteria for patient selection are: male patients under 60 years of age with osteoarthritis, good bone quality, no significant acetabular deformity, and a large diameter femoral head to accommodate a femoral component of 50 mm or larger. Selection of female patients for this procedure requires very careful consideration. • Metal-on-metal HRA should only be performed by surgeons who have appropriate training and who have acquired a high level of experience by performing a high annual volume of THAs and MOM HRAs. o Expert opinion, informed that the appropriate volume is considered to be performing at least 100 THAs and at least 20 HRAs per year. • There is evidence of increased cobalt and chromium levels in the blood and urine of patients who receive MOM HRA; however, there is no conclusive evidence that exposure to high metal ion levels has harmful biological consequences. As such, OHTAC recommends that patients receiving these implants be informed of the potential for exposure to metal ions, and that the adverse effects and long-term implications of elevated metal ion exposure in patients who receive these implants are not known at this time. • Since cobalt and chromium can pass the placental barrier, OHTAC recommends that non–MOM-bearing surfaces be used in women of childbearing ages who require hip arthroplasty.	Based on an HQO evidence-based analysis *(GRADE low to very low). (68)*
7.7 When bilateral joint replacements are required, they can be performed sequentially under the same anesthetic or staged over two separate hospitalizations. • The treatment decision should be at the surgeon's discretion. • The potential increased risk of mortality and pulmonary embolism associated with simultaneous bilateral replacements needs to be recognized, and appropriate patient selection and rationale should be applied.	**HQO Rapid Review** Simultaneous in comparison to staged bilateral TKA (see Rapid Review No. 2 in Appendix I): - A significant increase in 30-day mortality *(GRADE: very low)* - A significant increase in pulmonary embolism *(GRADE: very low)* - A significant decrease in deep infection *(GRADE: very low)*

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
7.8 The decision to use cemented or cementless fixation should be at the surgeon's discretion.	**HQO Rapid Review** Cemented in comparison to cementless fixation for THA (see Rapid Review No. 3 in Appendix I): - No significant difference in revisions (*GRADE: low*)
Infection Prevention	
7.9 There is insufficient evidence to make a recommendation for or against the use of ALBC for primary joint replacement.	**HQO Rapid Review** ALBC in comparison to plain bone cement for knee arthroplasty (see Rapid Review No. 4 in Appendix I): - 2 RCTs identified significantly lower infection rates among persons with and without diabetes *(GRADE: very low)* - 1 observational study found no significant difference in infection rates *(GRADE: very low)*
7.10 Routine antibiotic administration is recommended as a prophylaxis against infection. • It is recommended that patients receive 1 dose of antibiotic preoperatively and 3 subsequent doses postoperatively over the course of 24 hours.	Agrees with Bone and Joint Canada (*Expert Consensus*) (19), the NSW (*Grade A*) (17), and Dutch Guideline (*level 1 and 4*). (62)
7.11 The use of chlorhexidine for surgical site infection prevention should follow the Institute for Healthcare Improvement enhanced surgical practice recommendations.	Based on Expert Panel consensus with reference to the Institute for Healthcare Improvement Guideline on Enhanced Surgical Site Infection Prevention Bundle: Hip and Knee Arthroplasty. (65)
VTE Prevention	
7.12 Venous thromboembolism (VTE) prevention is recommended. • Care providers should consider following the American College of CHEST Physicians guidelines on the prevention of VTE in orthopedic surgery patients.	Based on Expert Panel consensus with reference to CHEST guidelines. (64)

Abbreviations: ALBC, antibiotic bone cement; RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Module 7: Implementation Considerations

Potential Levers	• Every hospital should have a surgical safety checklist that complies with Accreditation Canada requirements.

Module 8: Postoperative Care

This module identifies recommended practices for postoperative, inpatient, management subsequent to hip or knee replacement surgery. Recommended practices in areas such as pain management and thromboprophylaxis may overlap or be applied within earlier modules. The key areas of emphasis relate to pain management and early patient mobilization.

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
Pain Management	
8.1 A multimodal approach to postoperative pain management should be employed. • This may include systemic analgesics (both non-opioid and opioid), nerve blocks (peripheral or neuraxial), and/or local infiltration analgesia (LIA).	**HQO Rapid Review** Effectiveness of LIA for knee and hip arthroplasty (see Rapid Review No. 5 in Appendix I): - There are inconsistent results for the impact of LIA on pain *(GRADE: very low)* - There are inconsistent results for the impact of LIA on hospital length of stay *(GRADE: very low)*
Mobilization and Rehabilitation	
8.2 Early postoperative mobilization is recommended. • There should be input from a multidisciplinary rehabilitation team and a structured mobilization plan for postoperative rehabilitation.	Agrees with the NSW *(Grade B)* (17) and the BOA *(Expert Opinion). (7;8)*
8.3 The optimal intensity of rehabilitation during the acute hospitalization period is unknown.	**HQO Rapid Review** Higher intensity rehabilitation in comparison to lower intensity rehabilitation during the immediate acute care hospitalization period (see Rapid Review No. 6 in Appendix I): *For THA:* *Comparing twice daily PT to once daily PT among hip arthroplasty patients, there was:* - A statistically, but not clinically, significant improvement in functional status measured using the Iowa Level of Assistance score at 3 days after surgery and no significant difference at 6 days after surgery *(GRADE: moderate)* - No significant difference in hospital length of stay *(GRADE: very low)*

Recommendations	Contributing Sources for the Recommendations *(quality of evidence)*
	For TKA: *Comparing twice daily PT to once daily PT among knee arthroplasty patients, there was:* - No significant difference in hospital length of stay *(GRADE: low)*
8.4 Continuous passive motion is not recommended.	Agrees with Bone and Joint Canada's Supplemental Evidence Review *(suggestive evidence)* (19) and the NSW *(Grade A*). *(17)*

Abbreviations: PT, physiotherapy; RCT, randomized controlled trial.

Module 9: Post-Acute Care: Inpatient Rehabilitation, Home Care Rehabilitation, and Outpatient Rehabilitation

Post-acute care rehabilitation is a key component in overall patient recovery. This module describes the rehabilitation that patients receive after discharge from the hospital, which can be provided in the outpatient setting through hospital, community, and in-home resources, or in the inpatient setting among selected patients.

Recommendations	Contributing Sources to the Recommendations *(quality of evidence)*
9.1 Rehabilitation is required for successful recovery of patients after hip or knee replacement surgery. • Appropriate rehabilitation services need to be timely and accessible. • Rehabilitation requirements for hip replacement surgery may differ from those of knee replacement surgery.	Based on Bone and Joint Canada (*Expert Opinion*) (19) and modified by the Expert Panel.
9.2 The following OHTAC recommendation should be followed with regards to location of physiotherapy rehabilitation: • OHTAC recommends the health system support the move towards community-based physiotherapy after primary total knee or hip replacement and discharge from acute care. In regards to location of physiotherapy within the community, the health system should allow for flexibility, depending on the local care context and patients' needs. Current initiatives that are underway in the province to improve allocation of physiotherapy services for primary hip and knee replacement patients should be supported by the health care system.	Based on HQO evidence-based analysis and OHTAC recommendations (GRADE: *high). (69)*
9.3 All patients discharged home should be provided an independent home exercise program.	Based on Expert Panel consensus and agrees with Bone and Joint Canada (*Expert Opinion*). (19)
9.4 The following OHTAC recommendations should be considered with regards to patients who could attend outpatient physiotherapy clinics: • For patients who could attend an outpatient physiotherapy clinic, consideration may be given to a self-managed home exercise program with a physiotherapist monitoring through phone calls.	Based on 2005 HQO evidence-based analysis and OHTAC recommendations (GRADE: *low to moderate). (69)*
9.5 Patients should have access to the Community Care Access Centres (CCACs) for assessment of eligibility for supportive services. • CCAC eligibility algorithms should be standardized across the province.	Based on Expert Panel consensus and agrees with Bone and Joint Canada (*Expert Opinion*). (19)
9.6 Inpatient rehabilitation should be restricted to patients who meet specific eligibility criteria. • Eligibility criteria for inpatient rehabilitation should be standardized.	Based on Expert Panel consensus and agrees with Bone and Joint Canada (*Expert Opinion*). (19)
9.7 There is insufficient evidence to make a recommendation regarding the restricting of high-impact activities.	Agrees with Bone and Joint Canada's Supplemental Evidence Review *(Inconclusive Evidence)*. (19)

Follow-Up Period

9.8 Patients should have follow-up appointments with their surgical team after primary hip or knee replacement.

Based on Bone and Joint Canada *(Expert Opinion)* (19) and modified by the Expert Panel and agrees with NSW *(Grade D). (17)*

Module 9: Implementation Considerations

Barriers	• There is significant variation in access to and types of rehabilitation programs available to Ontarians depending on residence. • There is very little provincial level data on local availability for different forms of rehabilitation (outpatient clinics, home care, etc.). There is no provincial directory of the locations of rehabilitation programs. • There is incomplete provincial data on the number of patients enrolled in rehabilitation programs. • Hospitals are not required to report on outpatient rehabilitation clinic activity. This is a significant gap in provincial information systems; we know what percentage of patients go to inpatient rehabilitation and what percentage receive rehabilitation through CCACs, but not the percentage of patients who receive rehabilitation from outpatient clinics. • Key components of rehabilitation programs should be standardised so that all patients in the province receive access to standardized options for rehabilitation. • There is no defined provincial eligibility criteria for inpatient rehabilitation. • There is no consistent criteria for patient outcome measures; e.g., range of motion. • There is no standardized eligibility criteria for referral to inpatient rehabilitation.
Potential Levers	• Develop benchmark with results to be publicly reported. • Recently announced new funding for physiotherapy and rehabilitation/exercise services by CCACs to be clarified • Develop provincial minimum data set for patient outcome measures; e.g., range of motion. • Develop criteria for referrals to inpatient rehabilitation.

Performance Measurement

Following the identification of a set of recommended practices for the Primary Hip and Knee Replacement Episode of Care, the Expert Panel was asked to provide recommendations around performance measures aligned with the episode of care.

Implementation Considerations

The Primary Hip and Knee Replacement Episode of Care Expert Advisory Panel believes that implementation of best practices related to hip and knee care will require significant investment. The following points highlight some of the key issues for and barriers towards the successful implementation of the hip and knee best practices discussed:

1. It will not be possible to promote the movement of appropriate patients to community or ambulatory care and achieve the associated cost efficiencies without addressing out-of-hospital incentives for best practices and adequate outpatient rehabilitation services postdischarge.

2. A transitional approach to funding is recommended so as to enable the building of capacity in the community and to avoid the consequences of patients receiving no service.

3. A standardized province-wide joint replacement referral protocol and EHR to support protocol.

4. Development of province-wide coordinated intake process is required to ensure appropriate referrals are triaged to next available surgeon or to the patient's surgeon of choice.

5. When a referral is deemed inappropriate, centralized intake centres should notify the PCP to why the referral was turned down and provide alternatives for care.

6. Preoperative functional assessment should be used (e.g., WOMAC).

7. Transportation supports will need to be in place to support access to rehabilitation services, particularly when an outpatient- or facility-based rehabilitation program is the optimal model.

8. Provincial standards or protocols should be developed for nonsurgical management of patients and be easily accessible by PCPs.

9. Patient education materials should be standardized and available in multiple languages.

10. All hospitals providing joint replacement should align their pathways to the evidence-based recommendations made in this report.

11. All hospitals to adopt the forthcoming health transformation discharge planning standards.

12. Preoperative screening and diagnosis should align with provincial standards of appropriateness (see, for example, the HQO panel on preoperative diagnosis).

13. All hospitals should be required to have a surgical safety checklist that complies with Accreditation Canada requirements.

14. Provincial standardized criteria for referral to inpatient rehabilitation need to be developed and monitored.

15. Standardized outcomes measures for post-joint replacement rehabilitation should be developed (e.g., range of motion)

16. Key components of a rehabilitation program should be developed so that all patients receive access to rehabilitation whether at home, in community rehabilitation clinics, or in the hospital.

17. Access to the recently announced CCAC initiative for physiotherapy services in primary care and in patients' homes should be maximized.

18. Stakeholders have repeatedly raised concerns over using the top performing/best practice facilities as a benchmark for QBP in that some hospitals may be unfairly punished and not given the opportunity to improve.

Expert Panel Membership

HQO's Primary Hip and Knee Replacement Episode of Care Advisory Panel

Panel Member	Affiliation(s)	Appointment(s)
Panel Chair		
Dr James Waddell	St. Michaels Hospital; University of Toronto	Orthopaedic Surgeon Professor, Division of Orthopaedic Surgery
Orthopaedic Surgery		
Dr John Rudan	Queens University Kingston General Hospital	Head of Department of Surgery Orthopaedic Surgeon
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Dr Maurice Bent	North York General Hospital	Chief, Division Orthopedic Surgery
Dr David Backstein	Mount Sinai Hospital University of Toronto	Division Head of Orthopaedic Surgery Associate Professor
Dr Paul E. Beaulé	University of Ottawa	Professor of Surgery, Head of Adult Reconstruction
Dr Steven MacDonald	London Health Science Centre University of Western Ontario	Site Chief of Orthopaedic Surgery Professor, Division of Orthopaedic Surgery
Dr Mitchell Winemaker	Hamilton Health Sciences – Chief of Orthopedic Surgery	Juravinski Hospital McMaster University Associate Professor
Dr Andrew Van Houwellingen	Orthopaedic Surgeon	St. Thomas Elgin General Hospital
Primary Care		
Dr Tatiana Jevremovic	University of Western Ontario Fowler Kennedy Sport Medicine Clinic	Assistant Professor Department of Family Medicine
Dr Christopher Jyu	Rouge Valley Health System The Scarborough Hospital	Primary Care Lead
Internal Medicine		
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Anesthesiology		
Dr Nick Lo	St. Michael's Hospital University of Toronto	Staff Anesthesiologist Assistant Professor, Department of Anesthesiology

Panel Member	Affiliation(s)	Appointment(s)
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Geriatric Medicine		
Dr Anna Byszewski	The Ottawa Hospital Regional Geriatric Program of Eastern Ontario	Staff Geriatrician Full Professor, University of Ottawa
Physiotherapy and Rehabilitation		
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Raymond Kao	St. Michael's Hospital	Case Manager, Inpatient Mobility Program
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Executive Administration		
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Tiziana Silveri	North Bay Regional Health Centre	Vice President, Clinical Services
Rhona McGlasson	Bone and Joint Canada	Executive Director
Brenda Flaherty	Hamilton Health Sciences	EVP and Chief Operating Officer
Charissa Levy	GTA Rehab Network	Executive Director
Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

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Appendices

Appendix I: Rapid Reviews

1. Anesthesia Among Patients Undergoing Knee Arthroplasty: A Rapid Review
2. Simultaneous or Staged Bilateral Knee Arthroplasty: A Rapid Review
3. The Effectiveness of Cement in Primary Hip Replacements: A Rapid Review
4. Antibiotic-Laden Bone Cement for Primary Knee Arthroplasty: A Rapid Review
5. Local Infiltration Analgesia in Hip and Knee Arthroplasty: A Rapid Review
6. Intensity of Rehabilitation During the Acute Hospitalization Period After Hip or Knee Arthroplasty: A Rapid Review

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Anesthesia Among Patients Undergoing Knee Arthroplasty: A Rapid Review

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
GRADE	Grading of Recommendations Assessment, Development and Evaluation
NR	Not reported
RCT	Randomized controlled trial
SD	Standard deviation

Background

Objective of Analysis

The objective of this rapid review is to examine the safety and effectiveness of regional anesthesia versus general anesthesia among patients undergoing primary knee arthroplasty.

Clinical Need and Target Population

Anesthesia is required among patients undergoing knee arthroplasty. The 2 main categories of anesthesia are general and regional. According to definitions from the Canadian Anesthesiologists' Society, general anesthesia is a reversible state of complete unconsciousness with loss of memory, pain relief, and muscle relaxation induced by drugs typically administered intravenously or by inhaled induction. (1) Regional anesthesia is the injection of a local anesthetic to an area of the body close to a nerve or group of nerves that supply function or feeling to the area of body involved in an operation. (1)

When deciding what anesthesia is to be used, several factors are considered by the surgical team. With all things being equal, there is currently uncertainty over potential benefits or risks to patients who receive general versus regional anesthesia when undergoing knee arthroplasty.

Rapid Review

Research Question

What is the safety and effectiveness of regional anesthesia versus general anesthesia among patients undergoing primary knee arthroplasty?

Research Methods

Literature Search

A literature search was performed on April 19, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until April 19, 2013. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, until April 19, 2013
- systematic reviews, health technology assessments, and meta-analyses
- primary knee arthroplasty
- compared regional anesthesia to general anesthesia

Exclusion Criteria

- studies where results on outcomes of interest could not be abstracted
- case reports, editorials, letters, comments, and conference abstracts

Outcomes of Interest

- hospital length of stay
- mortality

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. The panel was composed of physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from the community.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to place the evidence produced by Health Quality Ontario into context and to provide advice on the appropriate clinical pathway for hip and knee arthroplasty in Ontario health care. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was used to assess the quality of the final selection of systematic reviews. (2) Primary studies were abstracted from the selected reviews and referenced for assessment of the 2 outcomes of interest.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group criteria. (3) The overall quality was determined to be very low, low, moderate, or high via a step-wise, structural method.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that can raise the quality of evidence were considered: large magnitude of effect, dose-response gradient, and accounting for all residual confounding factors. (3) For more detailed information, please refer to the latest series of GRADE articles. (3)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to the estimate of the effect;
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;
Low	Confidence in the effect estimate is limited—the true effect could be substantially different from the estimate of the effect;
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect.

Results of Literature Search

The database search yielded 457 citations published between January 1, 2008, and April 19, 2013 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One systematic review met the inclusion criteria. The reference lists of studies that were deemed topically relevant and health technology assessment websites were hand searched to identify any potentially relevant studies, and no additional citations were identified.

Quality Assessment of Reviews

As assessed by the AMSTAR score, the quality of the included review was a 7 of a possible 11 (see Appendix 2, Table A1).

Summary of Included Studies

The systematic review by Macfarlane et al was published in 2009 and included RCTs published between 1990 and 2008. (4) Its objective was to determine whether regional anesthesia improves patient outcomes after knee arthroplasty; it identified 28 studies with a total of 1,538 patients. (4) There was no meta-analysis or other qualitative summary of effect estimates. (4) The authors concluded that regional anesthesia reduced pain, morphine consumption, and opioid-related adverse effects. As well, it can reduce length of stay and aid in rehabilitation. (4) Additionally, the authors noted no difference in blood loss or in the length of surgery and insufficient evidence that anesthesia type affected mortality, cardiovascular morbidity or deep vein thrombosis, and pulmonary embolism. (4) The systematic review's scope was larger than the scope of interest for this rapid review, and therefore the reference list was hand searched to identify individual articles that met the review's inclusion criteria. This resulted in a final inclusion of 4 RCTs evaluating the 2 identified outcomes of interest summarized in Table 1. (5-8)

Table 1: Randomized Controlled Trials Assessing General Versus Regional Anesthesia

Author, Year	Population	Sample Size (Intervention/ Control)	Regional Anesthesia Group (Intervention)	General Anesthesia Group (Control)
Mitchell et al, 1991 (5)	Knee arthroplasty	72 (34/38)	Epidural anesthesia (pharmaceutical unspecified)	General anesthesia (sodium thiopental, succinylcholine, halogenated agent, and nitrous oxide in oxygen)
Moiniche et al, 1994 (6)	Hip or knee arthroplasty	Knee group: 20 (10/10)	Continuous epidural (bupivacaine plus morphine) for 48 hours post-surgery and oral piroxacam	General anesthesia and intramuscular opioid (midazolam, fentanyl, and pancuronium) and acetaminophen
Williams-Russo et al, 1995 (7)	Knee arthroplasty	262 (134/128)	Epidural (lidocaine or bupivicaine, and midazolam or fentanyl) and post-surgery epidural analgesia as requested	General anesthesia (thiopental sodium, fentanyl, vecuronium, and nitrous oxide) and post-surgery intravenous analgesia
Williams-Russo et al, 1996[a] (8)	Knee arthroplasty	178 (97/81)	Epidural (lidocaine or bupivicaine, and midazolam or fentanyl) and post-surgery epidural analgesia as requested	General anesthesia (thiopental sodium, fentanyl, vecuronium, and nitrous oxide) and post-surgery intravenous analgesia

[a]Subgroup of Williams-Russo et al, 1995 study (7) of patients who received thromboembolic prophylaxis.

Results for Outcomes of Interest

Mortality

One RCT examined mortality as an outcome of interest, with results described in Table 2.

Table 2: Mortality Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample Size	Results for Outcome of Mortality	Statistical Significance
Williams-Russo et al, 1995 (7)	262	2 months after surgery: Regional anesthesia group: 1 death General anesthesia group: 1 death	Not significant[a]

[a]Not reported in the publication, but based on a calculation of the odds ratio using the raw data presented.

No statistical analysis was provided for this outcome. An odds ratio calculation using the data provided in the publication showed no statistically significant difference between the study groups for the outcome of mortality (odds ratio 0.95, 95% confidence interval 0.06, 15.43). The GRADE for the quality of evidence was evaluated as very low; details are provided in Appendix 2, Table A2.

Hospital Length of Stay

The 4 RCTs all reported on hospital length of stay. Because of limitations in the data available, a meta-analysis was not conducted. Individual study results are described in Table 3. (5-8)

Table 3: Hospital Length of Stay Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample Size	Mean Length of Stay, Days (SD)		Statistical Significance
		Regional Anesthesia Group	General Anesthesia Group	
Mitchell et al, 1991 (5)	72	11.0 (NR)	10.4 (NR)	Not significant[a]
Moinische et al, 1994 (6)	20	12.0 (NR)	13.0 (NR)	Not significant[a]
Williams-Russo et al, 1995 (7)	262	12.7 (5.3)	12.7 (4.3)	Not significant[a]
Williams-Russo et al, 1996 (8)[b]	178	12.1 (4.5)	12.7 (4.3)	*P* = 0.27

Abbreviations: NR, not reported; SD, standard deviation.
[a] As reported in publication, no *P* value was published.
[b] Subgroup of Williams-Russo et al 1995 study (7) of patients who received thromboembolic prophylaxis.

All studies identified no statistically significant difference in the hospital length of stay among knee arthroplasty patients who received regional anesthesia versus those who received general anesthesia. The GRADE for the quality of evidence was evaluated as very low; details are provided in Appendix 2, Table A2.

The Canadian Institute for Health Information stated in 2006 that the average length of stay for Ontario patients undergoing hip or knee replacements was 7 days for men and 8 for women. (9) This was further placed into context by the Expert Advisory Panel, who stated that the current average length of stay for these patients in Ontario is closer to 4 days. Consequently, the evidence on the effect of regional versus

general anesthesia on hospital length of stay among patients undergoing primary knee arthroplasty in Ontario is considered insufficient.

Addendum

On the advice of the Expert Panel, a pivotal observational study comparing regional to general anesthesia in primary total joint arthroplasty had recently been published. These results, along with the very low quality of evidence obtained from the original rapid review, prompted a decision to add and evaluate observational data.

The original literature search was revisited in light of the same inclusion and exclusion criteria as the original rapid review, with the modification of limiting to the last 2 years and including observational studies (search dates from January 1, 2011, to April 19, 2013). Two observational studies were identified, in addition to the 1 study identified by the Expert Panel that was published 1 month after the original literature search dates; 3 observational studies are included in this addendum.

Table 4 briefly describes the included studies. Of the 3 studies 2 used the same administrative data source; the Stundner et al (10) publication is a subgroup of the study by Memtsoudis et al (11).

Table 2: Summary of Observational Studies

Author, Year	Location	Data Source	Population	Sample Size	Study groups
Memtsoudis, 2013 (11)	USA	Premier Perspective, Inc.[a]	All primary lower extremity joint arthroplasty conducted 2006–2010 (TKAs and THAs)	356,028 TKAs; 172,467 THAs	3 groups: -neuraxial anesthesia general anesthesia neuraxial + general anesthesia
Stundner, 2012 (10)	USA	Premier Perspective, Inc.[a]	Bilateral TKAs conducted 2006–2010	15,687	3 groups: -neuraxial anesthesia general anesthesia neuraxial + general anesthesia
Pugely, 2013 (12)	USA	ACS NSQIP[b]	TKAs 2005–2010	14,052	Spinal anesthesia General anesthesia

Abbreviations: ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a]Includes data from approximately 400 acute care hospitals throughout the United States.

[b]Includes data from 258 hospitals throughout the United States.

Addendum Results for Outcomes of Interest

Mortality

The Memtsoudis et al (11) study identified a statistically significant decrease in 30-day mortality among patients who underwent TKA and received regional anesthesia compared with those who received general anesthesia (Table 5). The body of evidence for the outcome of 30-day mortality was evaluated as low quality (Appendix 3, Table A4).

Table 3: 30-Day Mortality Results From Observational Studies Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample size (intervention/ control)	Results
Memtsoudis, 2013 (11)	28,426 regional/194,682 general anesthesia	Odds ratio[a] 0.55 (95% confidence interval 0.32–0.93)[b]

[a] Multivariate weighted logistic regression adjusted for age, sex, race, admission type, payer type, hospital size, hospital location, hospital teaching status, surgical pathology, and comorbidity burden.

[b] Calculated inverse of effect estimate reported in original publication.

Given the limitations of the data reported, neither Stundner et al (10) nor Pugely et al (12) were included in the analysis. Both studies reported only unadjusted numbers for the outcome of mortality, and neither found a statistically significant difference between the regional and general anesthesia study groups.

Length of Stay

Stundner et al (10) identified no statistically significant difference between groups in hospital length of stay (Table 6). Evidence for the outcome of length of stay was evaluated as low quality (Appendix 3, Table A4).

Table 4: Length of Stay Results From Observational Studies Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample size (intervention/ control)	Results
Stundner, 2012 (10)	1,066 regional/12,567 general anesthesia	Odds ratio[a] 1.07 (95% confidence interval 0.91–1.26)

[a] Adjusted for age, sex, race, and comorbidity burden.

Memtsoudis et al (11) did not report on length of stay and, due to the limitations of the data reported, the study by Pugely et al (12) was excluded from the current analysis. Pugely et al (12) reported only unadjusted numbers for the outcome of length of stay and reported a statistically significant decrease among patients who received regional versus general anesthesia.

Conclusions

From the examination of 1 systematic review of randomized controlled trials as part of the rapid review:

- Based on very low quality of evidence, there was no significant difference in mortality for patients who received regional anesthesia versus those who received general anesthesia for primary knee arthroplasty.

- Based on very low quality of evidence, there was no significant difference in hospital length of stay for patients who received regional anesthesia versus those who received general anesthesia for primary knee arthroplasty.

From the examination of observational studies as part of the addendum to the rapid review:

- Based on low-quality evidence, there was a statistically significant decrease in 30-day mortality among patients who received regional versus general anesthesia for primary knee arthroplasty.

- Based on low-quality evidence, there was no significant different in hospital length of stay among patients who received regional versus general anesthesia for primary knee arthroplasty.

Acknowledgements

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Expert Advisory Panel for Health Quality Ontario on Episodes of Care for Primary Hip/Knee Replacement

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Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

Appendices

Appendix 1: Literature Search Strategies

Search date: April 19, 2013
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; Centre for Reviews and Dissemination
Limits: 2008-current; English; removal of case reports, editorials, letters, comments, conference abstracts
Filters: none

Database: Embase 1980 to 2013 Week 15, Ovid MEDLINE(R) 1946 to April Week 2 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 18, 2013
Search Strategy:

#	Searches	Results
1	exp Arthroplasty, Replacement, Knee/ use mesz or Arthroplasty, Replacement/ use mesz	14761
2	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	32528
3	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	47547
4	or/1-3	51194
5	exp Anesthesia, Conduction/ use mesz	50849
6	exp regional anesthesia/ use emez or exp epidural anesthesia/ use emez or exp local anesthesia/ use emez or exp spinal anesthesia/ use emez	90421
7	(((an?esthet* or an?esthesia) adj4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*).ti,ab.	127244
8	or/5-7	198034
9	4 and 8	2143
10	limit 9 to english language	1949
11	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congresses.pt.	3976280
12	Case Report/ or Comment/ or Editorial/ or Letter/ or conference abstract.pt.	6638882
13	or/11-12	6709824
14	10 not 13	1342
15	limit 14 to yr="2008 -Current"	660
16	remove duplicates from 15	437

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees	1279
#2	MeSH descriptor: [Arthroplasty, Replacement] explode all trees	2541
#3	MeSH descriptor: [Knee Prosthesis] explode all trees	501
#4	((knee* near/2 (replacement* or arthroplast*)) or (knee* near/2 prosthes?s) or TKR):ti,ab,kw (Word variations have been searched)	2211
#5	#1 or #2 or #3 or #4	3444
#6	MeSH descriptor: [Anesthesia, Conduction] explode all trees	6954
#7	(((an?esthet* or an?esthesia) near/4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*):ti (Word variations have been searched)	2815
#8	(((an?esthet* or an?esthesia) near/4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*):ab (Word variations have been searched)	4963
#9	#6 or #7 or #8	10133
#10	#5 and #9 from 2008 to 2013	131

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR Arthroplasty, Replacement, Knee EXPLODE ALL TREES	242
2	MeSH DESCRIPTOR Arthroplasty, Replacement EXPLODE ALL TREES	480
3	MeSH DESCRIPTOR Knee Prosthesis EXPLODE ALL TREES	60
4	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR)	429
5	#1 OR #2 OR #3 OR #4	666
6	MeSH DESCRIPTOR Anesthesia, Conduction EXPLODE ALL TREES	226
7	(((an?esthet* or an?esthesia) adj4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*)	453
8	#6 OR #7	454
9	#5 AND #8	24
10	(#9) FROM 2008 TO 2013	15

Appendix 2: Quality Assessment Tables

Table A1: AMSTAR Score of Reviews

Author, Year	AMSTAR score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
Macfarlane et al, 2009 (4)	7	✓		✓			✓	✓	✓	✓		✓

Abbreviation: AMSTAR, Assessment of Multiple Systematic Reviews.
[a]Details of AMSTAR method are described in Shea et al. (2)

Table A2: GRADE Evidence Profile for Comparison of Regional Anesthesia Versus General Anesthesia

No. of Studies by Design	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Mortality							
1 RCT	Serious limitations (−1)	No serious limitations	No serious limitations	Very serious limitations (−2)[d]	Undetected	None	⊕ Very low
Length of Stay							
4 RCTs	Very serious limitations (−2)	No serious limitations	Serious limitations (−1)[b]	Serious limitations (−1)[c]	Undetected	None	⊕ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; No., number; RCT, randomized controlled trial.
[a]Details on risk of bias are described in Table A3.
[b]Because average hospital length of stay differed, the Episode of Care Expert Advisory Panel considered the body of literature different from the current Ontario context.
[c]Limited data available make confidence intervals around an effect estimate immeasureable.
[d]Sample size does not meet optimal information size criteria, and confidence intervals around the odds are wide.

Table A3: Risk of Bias Among Randomized Controlled Trials for Comparison of Regional Versus General Anesthesia

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Mitchell et al, 1991 (5)	Limitations[a]	Limitations[b]	No limitations	No limitations	Limitations[c]
Moiniche et al, 1994 (6)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Williams-Russo et al, 1995 (7)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Williams-Russo et al, 1996 (8)[d]	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations

[a]Health care providers could not be blinded to treatment group and as a result might have biased evaluation of subjective outcomes (e.g., pain).
[b]Patients could not be blinded to their study group of regional or general anesthesia and as a result might have biased evaluation of subjective outcomes (e.g., pain). Length of stay could be influenced by patients' pain.
[c]Treatment protocols differed by sex, but results showed no indication of bias between study groups. Men received 650 mg of acetylsalicylic acid while women were given low-dose warfarin the night before surgery.
[d]Subgroup of Williams-Russo et al,1995 study (7) of patients who received thromboembolic prophylaxis.

Appendix 3: Quality Assessment Tables for Addendum

Table A4: GRADE Evidence Profile for Comparison of Regional Versus General Anesthesia in Observational Studies

No. of Studies (Design)	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Mortality							
1 Observational	No serious limitations	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Length of Stay							
1 Observational	No serious limitations	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low

[a]Details on risk of bias are available in Table A5

Table A5: Risk of Bias Among Observational Studies for Comparison of Regional Versus General Anesthesia

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
Stundner et al, 2012 (10)	No limitations	No limitations	No limitations	No limitations [a]	No limitations
Memtsoudis et al, 2013 (11)	No limitations	No limitations	No limitations	No limitations [b]	No limitations

[a]Multivariate regression model and propensity score matching was conducted for evaluation of certain outcomes.
[b]Multivariate regression model was conducted for evaluation of certain outcomes.

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Simultaneous or Staged Bilateral Knee Arthroplasty: A Rapid Review

Evidence Development and Standards Branch at
Health Quality Ontario

November 2013

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All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

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This report was prepared by Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee *and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to Health Quality Ontario. It is possible that relevant scientific findings may have been reported since the completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications:* http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
OR	Odds ratio
TKA	Total knee arthroplasty

Background

Objective of Analysis

The objective of this analysis was to determine the safety of simultaneous bilateral knee arthroplasty compared to staged bilateral knee arthroplasty.

Clinical Need and Target Population

Individuals with osteoarthritis or rheumatoid arthritis of both knees may require replacement of the affected joints using bilateral knee arthroplasty. (1) Planned bilateral knee arthroplasty can be performed in a simultaneous or staged manner. (1)

Technology/Technique

Simultaneous bilateral knee arthroplasty refers to surgery conducted on both knees at the same time, with a single hospitalization and anaesthesia; it can be performed on both knees at once using 2 surgical teams or sequentially with 1 surgical team. *Staged bilateral knee arthroplasty* refers to a process involving 2 separate procedures and 2 hospitalizations. With staged bilateral knee arthroplasty, the interval between procedures can range from a few days to several months. Whether bilateral knee arthroplasty should be performed in a simultaneous rather than a staged manner remains controversial. (2;3)

Rapid Review

Research Question

What is the safety of simultaneous bilateral knee arthroplasty compared to staged bilateral knee arthroplasty?

Research Methods

Literature Search

Search Strategy

A literature search was performed on August 2, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, and EBM Reviews for studies published from January 1, 2007, to August 2, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2007, and August 2, 2013
- systematic reviews, meta-analyses, and health technology assessments
- bilateral knee arthroplasty population
- studies comparing simultaneous bilateral knee arthroplasty to staged bilateral knee arthroplasty
- 1 or more outcomes of interest

Exclusion Criteria

- studies comparing to unilateral knee arthroplasty

Outcomes of Interest

- mortality
- pulmonary embolism
- deep infection

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community laboratories.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for hip and knee arthroplasty in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (4)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (5) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (5) For more detailed information, please refer to the latest series of GRADE articles. (5)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 139 citations published between January 1, 2007, and August 2, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Three systematic reviews with meta-analyses met the inclusion criteria. The reference lists of the included studies were hand-searched to identify other relevant studies, but no additional citations were identified. The 3 systematic reviews are summarized in Table 1.

Table 1: Summary of Systematic Reviews

Author, Year	Study Selection Criteria	Number of Studies Included	AMSTAR Score[a]
Fu et al, 2013 (6)	Inclusions: published 1965–2012; simultaneous bilateral TKA and staged bilateral TKA; osteoarthritis or rheumatoid arthritis in both knees; severe pain unrelieved by conventional therapy Exclusions: primary trauma or knee infection; TKA or revision surgery	18 retrospective comparative studies	5
Hu et al, 2011 (7)	Inclusions: published 1980–2010; mortality and morbidity of simultaneous bilateral TKA with staged bilateral TKA Exclusions: simultaneous and staged groups not in same article; data duplicated; demographic background not similar; usable data not reported	14 prospective or retrospective case-control studies	5
Restropo et al, 2007 (8)	Inclusions: published up to 2005, safety of simultaneous bilateral TKA versus staged bilateral TKA; any diagnosis Exclusions: none stated	18 studies (type not specified)	6

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; TKA, total knee arthroplasty.
[a]Maximum possible score is 11.

Upon further review, the study by Restropo et al (8) was excluded, as it was the least recent and included unilateral total knee arthroplasty (TKA) in the staged bilateral TKA group. The remaining 2 studies had poor AMSTAR ratings with methodological flaws (Appendix 2). Given that both remaining studies had similar AMSTAR scores, Fu et al (6) was selected for inclusion in this rapid review, as it was the most recent and the most comprehensive.

Mortality

Mortality within 30 days after surgery was the primary endpoint reported in the review by Fu et al. (6) Thirteen of the 18 studies evaluated mortality, of which 7 provided estimable data for meta-analysis. Results from the studies and meta-analysis are presented in Table 2. Overall, the meta-analysis identified a significant increase in 30-day mortality among patients receiving simultaneous bilateral TKA compared to staged bilateral TKA ($P < 0.001$), but significant statistical heterogeneity was observed ($P = 0.009$). Although the methods stated that a random effects model would be used, the authors inappropriately used a fixed-effects model for this outcome. The GRADE for this body of evidence was very low.

Table 2: 30-Day Mortality With Simultaneous Bilateral TKA Compared to Staged Bilateral TKA

Author, Year	Number of Studies	Number of Patients (Simultaneous/ Staged)	30-Day Mortality Findings	Summary Estimate for Mortality OR (95% CI)	I^2, %
Fu et al, 2013 (6)	7	26,169/77,951	5 studies found a nonsignificant difference between groups 2 studies found a significant increase in 30-day mortality with simultaneous bilateral TKA	2.25 (1.87–2.72)	73

Abbreviations: CI, confidence interval; OR, odds ratio; TKA, total knee arthroplasty.

A sensitivity analysis was conducted by the authors, and it identified the largest observational study as the primary source of statistical heterogeneity. Removal of this study resulted in a nonsignificant difference in mortality between the 2 groups (odds ratio, 1.35; 95% confidence interval, 0.98–1.85; $P = 0.07$) and no significant statistical heterogeneity ($I^2 = 3\%$). However, a clear explanation for the potential clinical heterogeneity was not identified, and no additional subgroup analyses were considered.

Overall, the analyses of mortality were likely biased toward healthier patients in the staged TKA group, as mortality rates were calculated based on the number of individuals who had completed 2 TKA surgeries, requiring patients to survive the first procedure to be included in the analysis.

Pulmonary Embolism

Results of the Fu et al (6) meta-analysis on pulmonary embolism are presented in Table 3. The authors found a significant increase in the risk of pulmonary embolism among patients receiving simultaneous bilateral TKA compared to staged bilateral TKA ($P = 0.005$). The authors stated that all included studies routinely used thromboprophylaxis, but no information regarding type or duration of therapy was provided. The start and total length of follow-up across studies was not provided, and may have differed between the simultaneous and staged groups. The GRADE for this body of evidence was very low.

Table 3: Pulmonary Embolism With Simultaneous Bilateral TKA Compared to Staged Bilateral TKA

Author, Year	Number of Studies	Number of Patients (Simultaneous/ Staged)	Pulmonary Embolism Findings	Summary Estimate for Pulmonary Embolism OR (95% CI)	I^2, %
Fu et al, 2013 (6)	9	14,553/24,600	8 studies found a nonsignificant difference between groups 1 study found a significant increase in pulmonary embolism with simultaneous bilateral TKA	1.39 (1.11–1.76)	0

Abbreviations: CI, confidence interval; OR, odds ratio; TKA, total knee arthroplasty.

Deep Infection

A deep infection was defined by Fu et al (6) as any infection that occurred inside the knee joint and sometimes required removal of the prosthesis. Results from the meta-analysis on deep infection are presented in Table 4. Overall, there was a statistically significant decrease in deep infections among patients receiving simultaneous bilateral TKA compared to staged bilateral TKA ($P < 0.001$). The start and total length of follow-up was not provided, and may have differed between the simultaneous and staged groups. The GRADE for this body of evidence was very low.

Table 4: Deep Infection With Simultaneous Bilateral TKA Compared to Staged Bilateral TKA

Author, Year	Number of Studies	Number of Patients[a]	Deep Infection Findings	Summary Estimate for Deep Infection OR (95% CI)	I^2, %
Fu et al, 2013 (6)	7	38,743	No forest plot provided	0.52 (0.42–0.64)	0

Abbreviations: CI, confidence interval; OR, odds ratio; TKA, total knee arthroplasty.
[a]The number of patients in each group was not provided.

Limitations of Included Studies

The systematic review by Fu et al (6) and the studies included in the meta-analyses had potential methodological limitations that warrant caution in the interpretation of results. First, the assessment of simultaneous and staged bilateral surgery was limited to retrospective cohort studies, so that only observed—rather than planned—procedures were captured. This limitation may result in a bias toward healthier individuals, since those who had planned a staged TKA but did not complete the second procedure due to death or a serious complication would be misclassified as a unilateral TKA. (9) Additionally, no information was provided on how bilateral TKAs were identified in individual studies, or the period of time accepted or observed between staged bilateral TKAs.

The length of follow-up for pulmonary embolism and deep infection was not provided, and it is unclear whether these outcomes were assessed as cumulative events occurring after the first and second hospitalization in the staged bilateral TKA group, or if they were measured only after the second hospitalization. As a result, follow-up periods may differ between study arms or between individual studies.

Furthermore, no information on patient comorbidities was provided, and meta-analyses were conducted using raw data from the individual studies, eliminating any original analyses that may have adjusted for patient-level factors. Additionally, fixed- and random-effects models were inappropriately applied to the meta-analyses, and differed from the planned analyses outlined in the methods section of the review.

Conclusions

Based on 1 systematic review with methodological flaws, the following conclusions were made related to the safety of simultaneous bilateral TKA compared to staged bilateral TKA (very low quality of evidence):

- There was a significant increase in 30-day mortality.
- There was a significant increase in pulmonary embolism.
- There was a significant decrease in deep infections.

Acknowledgements

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Expert Panel for Health Quality Ontario: Episodes of Care for Primary Hip/Knee Replacement

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Dr John Rudan	Queens University Kingston General Hospital	Head of Department of Surgery Orthopaedic Surgeon
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Dr Maurice Bent	North York General Hospital	Chief, Division Orthopedic Surgery
Dr David Backstein	Mount Sinai Hospital University of Toronto	Division Head of Orthopaedic Surgery Associate Professor
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Deborah Marie Kennedy	Sunnybrook Holland Orthopaedic and Arthritic Centre	Manager, Rehabilitation and MSK Program Development
Raymond Kao	St. Michael's Hospital	Case Manager, Inpatient Mobility Program
Dr Peter Nord	Providence Healthcare Foundation University of Toronto	Vice President, Chief Medical Officer and Chief of Staff
Executive Administration		
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Tiziana Silveri	North Bay Regional Health Centre	Vice President, Clinical Services
Rhona McGlasson	Bone and Joint Canada	Executive Director
Brenda Flaherty	Hamilton Health Sciences	EVP and Chief Operating Officer
Charissa Levy	GTA Rehab Network	Executive Director
Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

Appendices

Appendix 1: Literature Search Strategies

Limits: 2007-current; English
Filters: Meta-analyses, systematic reviews and health technology assessments

Database: EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 2013>, EBM Reviews - ACP Journal Club <1991 to July 2013>, EBM Reviews - Database of Abstracts of Reviews of Effects <2nd Quarter 2013>, EBM Reviews - Cochrane Central Register of Controlled Trials <June 2013>, EBM Reviews - Cochrane Methodology Register <3rd Quarter 2012>, EBM Reviews - Health Technology Assessment <3rd Quarter 2013>, EBM Reviews - NHS Economic Evaluation Database <3rd Quarter 2013>, Embase <1980 to 2013 Week 30>, Ovid MEDLINE(R) <1946 to July Week 4 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <August 01, 2013>
Search Strategy:
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1 exp Arthroplasty, Replacement, Knee/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed (17811)
2 exp knee arthroplasty/ use emez or exp Knee Prosthesis/ (34513)
3 ((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp. (52919)
4 or/1-3 (57031)
5 exp Time Factors/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed (1054412)
6 exp time/ use emez (510791)
7 (bilateral* or simultan* or staged or sequen* or stagger* or synchron* or same day or double* or BTKA or STKA).mp. (5105252)
8 or/5-7 (6498118)
9 4 and 8 (8291)
10 Meta Analysis.pt. (46030)
11 Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed (55115)
12 Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez (85751)
13 (meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (376467)
14 ((health technolog* or biomedical technolog*) adj2 assess*).ti,ab. (4988)
15 or/10-14 (430094)
16 9 and 15 (240)
17 limit 16 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained] (237)
18 limit 17 to yr="2007 -Current" [Limit not valid in DARE; records were retained] (180)
19 remove duplicates from 18 (139)

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Scores of Included Systematic Reviews

Author, Year	AMSTAR Score	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Fu et al, 2013 (6)	5	✓	✓	✓	✗	✗	✗	✗	✓	✗	✗	✓
Hu et al, 2011 (7)	5	✗	✗	✓	✗	✗	✗	✗	✓	✓	✓	✓
Restrepo et al, 2007 (8)	6	✓	✓	✓	✓	✗	✗	✗	✗	✓	✗	✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.

[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al. (4)

Table A2: GRADE Evidence Profile for Comparison of Simultaneous Bilateral TKA and Staged Bilateral TKA

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
30-Day Mortality							
7 (observational)	Very serious limitations (–2)[a]	Serious limitations (–1)[b]	No serious limitations	No serious limitations	Undetected	None	⊕ Very Low
Pulmonary Embolism							
9 (observational)	Very serious limitations (–2)[ac]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very Low
Deep Infection							
7 (observational)	Very serious limitations (–2)[ac]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; TKA, total knee arthroplasty.

[a]Based on the systematic review by Fu et al, (6) all included studies were retrospective cohorts with poor methodological quality. Data on patient comorbidities was not provided, and all meta-analyses were conducted based on raw data from the original studies, therefore not controlling for confounding and lacking adjustment in statistical analyses. Staged bilateral knee arthroplasties were biased toward individuals who survived the first surgery and had a second surgery, therefore not accounting for individuals who died prior to the second surgery or who did not adhere to the planned treatment.

[b]Significant statistical heterogeneity was observed in the meta-analysis, with no clear account of potential subgroups.

[c]It is unclear whether complications in the staged bilateral TKA group were measured from the first or second hospitalization, and therefore may be longer than in the simultaneous bilateral TKA group.

References

(1) British Orthopaedic Association. Knee replacement: a guide to good practice [Internet]. London: British Orthopaedic Association; 1999 [cited 2013 Aug 16]. 24 p. Available from: http://www.boa.ac.uk/Publications/Documents/tkr_good_practice.pdf.

(2) Parvizi J, Rasouli MR. Simultaneous-bilateral TKA: double trouble - affirms. J Bone Joint Surg. 2012;94(11 Suppl A):90-2.

(3) Sculco TP, Sculco PK. Simultaneous-bilateral TKA: double trouble - opposes. J Bone Joint Surg. 2012;94(11 Suppl A):93-4.

(4) Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7(10):1-7.

(5) Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr; 64(4):380-2.

(6) Fu D, Li G, Chen K, Zeng H, Zhang X, Cai Z. Comparison of clinical outcome between simultaneous-bilateral and staged-bilateral total knee arthroplasty: a systematic review of retrospective studies. J Arthroplasty. 2013;28(7):1141-7.

(7) Hu J, Liu Y, Lv Z, Li X, Qin X, Fan W. Mortality and morbidity associated with simultaneous bilateral or staged bilateral total knee arthroplasty: a meta-analysis. Arch Orthop Trauma Surg. 2011;131(9):1291-8.

(8) Restrepo C, Parvizi J, Dietrich T, Einhorn TA. Safety of simultaneous bilateral total knee arthroplasty: a meta-analysis. J Bone Joint Surg. 2007;89(6):1220-6.

(9) Kim S, Meehan JP, White R. Operative risk of staged bilateral knee arthroplasty is underestimated in retrospective studies. J Arthroplasty. 2011;26(8):1198-204.

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The Effectiveness of Cement in Primary Hip Replacements: A Rapid Review

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

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In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This report was prepared by Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee *and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to Health Quality Ontario. It is possible that relevant scientific findings may have been reported since the completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications:* http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
RCT	Randomized controlled trial

Background

Objective of Analysis

The objective of this rapid review was to examine the effectiveness of cemented versus uncemented fixation components in primary hip arthroplasty.

Clinical Need and Target Population

Primary hip replacements may be conducted using cemented, uncemented or hybrid (a combination of cemented and uncemented) fixation components. (1) Cemented fixation was once more broadly used in primary hip replacements, but according to recent surveys, uncemented fixation has been adopted to varying degrees around the world. (2)

In Canada, the use of uncemented fixation had risen to 82% of all primary total hip arthroplasties by 2010, (2) in contrast to other countries such as Sweden, where only 15% of primary total hip arthroplasties used uncemented fixation techniques. (2) It remains uncertain whether there are significant differences in revision rates between the 2 fixation techniques.

Rapid Review

Research Question

What is the effectiveness of cemented versus uncemented fixation components in primary hip arthroplasty?

Research Methods

Literature Search

A literature search was performed on July 9, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, and EBM Reviews for studies published from January 1, 2008, to July 9, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2008, and July 9, 2013
- systematic reviews, meta-analyses, and health technology assessments
- primary hip arthroplasty
- comparing cemented versus uncemented fixation

Exclusion Criteria

- studies from which results on outcomes of interest could not be abstracted

Outcome of Interest

- revisions

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from the community.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for hip and knee arthroplasty in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (3) Primary studies were abstracted from the selected reviews and referenced for quality assessment of the body of the evidence for the outcomes of interest.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (4) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (4) For more detailed information, please refer to the latest series of GRADE articles. (4)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 41 citations published between January 1, 2008, and July 9, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Four systematic reviews met the inclusion criteria. The reference lists of the included studies were hand-searched to identify other relevant studies, but no additional citations were identified.

Quality Assessment of Systematic Reviews

The included systematic reviews are summarized in Table 5. The AMSTAR scores of the identified reviews ranged from 7 to 9 out of a possible 11 (Appendix 2). (3)

Table 5: Summary of Included Systematic Reviews

Author, Year	Search Dates	Design of Included Studies	Inclusion Criteria	AMSTAR (out of 11)
Abdulkarim et al, 2013 (5)	Unclear	RCTs	Studies that examined primary total hip replacement in patients ≥ 18 years	8
Pakvis et al, 2011 (6)	1980–2009	RCTs and comparative cohort studies with ≥ 12 months' follow-up	Studies that examined fixation of acetabular components among patients with the indication of primary or secondary osteoarthritis for total hip arthroplasty	7
Toossi et al, 2013 (7)	Up to 2011[a]	Prospective or retrospective studies with ≥ 10 years' follow-up	Studies of primary total hip arthroplasty that examined acetabular components. Studies of revisions to total hip arthroplasty and studies that reported only revisions of stems were excluded	7
Voigt et al, 2012 (8)	Up to 2011[a]	RCTs	Studies of primary hip implant in patients with osteoarthritis or rheumatoid arthritis that examined fixation of cemented all-polyethylene versus uncemented metal-backed acetabular components while using the same femoral component	9

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; RCT, randomized controlled trial.
[a]No start date limit applied.

Upon further review, 3 of the reviews were excluded because they limited their search and findings to an examination of the use of cement in the fixation of the acetabular components only. (6-8) For the purposes of this rapid review, only the Abdulkarim et al review was included. (5)

Results for the Outcome of Interest

Revisions

The systematic review by Abdulkarim et al (5) included 9 RCTs published between 1991 and 2006; of those, 6 reported on revisions in primary total hip replacement. Based on information published in the systematic review, (5) the findings of the 6 RCTs (9-14) are summarized in Table 6.

Table 6: Revisions in Primary Total Hip Replacement

Author, Year	Location	Follow-up	Sample Size	Intervention Versus Control	Risk Ratio (95% CI)
Kärrholm et al, 1994 (9)	Sweden	2 years	64	Cemented stem versus uncemented stem (both groups used uncemented acetabular components)	1.10 (0.22–5.52)
Laupacis et al, 2002 (10)	Canada	6.3 years	250	Cemented total hip prosthesis versus uncemented total hip prosthesis	2.20 (0.86–5.61)
Önsten et al, 1994 (11)	Sweden	2 years	60	Cemented socket versus uncemented socket (both groups used cemented stem components)	0.33 (0.01–7.87)
Reigstad et al, 1993 (12)	Norway	5 years	120	Cemented total hip prosthesis versus uncemented total hip prosthesis	0.14 (0.01–2.71)
Ström et al, 2006 (13)	Sweden	8 years	45	Cemented stem versus uncemented stem (both groups used uncemented acetabular components)	0.32 (0.01–7.45)
Wykman et al, 1991 (14)	Sweden	5 years	180	Cemented total hip prosthesis versus uncemented total hip prosthesis	1.57 (0.86–2.87)

Abbreviations: CI, confidence interval.

When results were pooled (all studies and a subgroup of studies with more than 5 years' follow-up), the review found no statistically significant difference in revisions between cemented and uncemented fixation in total hip replacement (Table 7). (5)

Table 7: Pooled Effect Estimates, Revisions

Number of Studies	Number of Studies per Intervention Pairing	Total Sample Size	Pooled Effect Estimate, Risk Ratio (95% CI)
All Included Studies			
6 RCTs	3 RCTs examining cement in stem and cup 2 RCTs examining cement in stem (both arms used uncemented acetabular components) 1 RCT examining cement in acetabular components (both arms used cemented stems)	719	1.44 (0.88–2.87)
Studies With ≥ 5 Years' Follow-up			
4 RCTs	3 RCTs examining cement in stem and cup 1 RCT examining cement in stem (both arms used uncemented acetabular components)	595	1.43 (0.70–2.93)

Abbreviations: CI, confidence interval; RCT, randomized controlled trial.

The quality of this body of evidence was low (Appendix 2).

Conclusions

Based on low quality of evidence, there was no statistically significant difference in revisions between cemented and uncemented fixation for primary hip arthroplasty.

Acknowledgements

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Expert Panel for Health Quality Ontario: Episode of Care for Primary Hip/Knee Replacement

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Appendices

Appendix 1: Literature Search Strategies

Search date: July 9, 2013
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; All EBM Databases
Limits: 2008-current; English
Filters: Meta-analyses, systematic review and heath technology assessments

Database: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to May 2013, EBM Reviews - ACP Journal Club 1991 to June 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2013, EBM Reviews - Cochrane Central Register of Controlled Trials June 2013, BM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 2nd Quarter 2013, EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2013, Embase 1980 to 2013 Week 27, Ovid MEDLINE(R) 1946 to June Week 4 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations July 08, 2013
Search Strategy:

#	Searches	Results
1	exp Arthroplasty, Replacement, Hip/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	22099
2	exp hip arthroplasty/ use emez or exp Hip Prosthesis/	56810
3	((hip* adj2 (replacement* or arthroplast* or resurfac*)) or ((femoral head* or hip*) adj2 prosthes?s) or THR).mp.	118853
4	or/1-3	123459
5	exp Bone Cements/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	18340
6	exp Bone Cement/ use emez	10270
7	exp Cementation/	8260
8	(((bone* or orthop?edic* or fixation or arthroplast*) adj2 (paste* or glue* or cement*)) or cementation).ti,ab.	18028
9	or/5-8	43418
10	4 and 9	10744
11	Meta Analysis.pt.	45649
12	Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	54613
13	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	83518
14	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	369062
15	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	4888
16	or/11-15	422354
17	10 and 16	143
18	limit 17 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	127
19	limit 18 to yr="2008 -Current" [Limit not valid in DARE; records were retained]	74
20	remove duplicates from 19	45

Appendix 2: Evidence Quality Assessment

Table A1: AMSTAR Scores of Included Systematic Reviews

Author, Year	AMSTAR Score[a]	(1) Provided Study Design	(2) Duplicate Study Selection	(3) Broad Literature Search	(4) Considered Status of Publication	(5) Listed Excluded Studies	(6) Provided Characteristics of Studies	(7) Assessed Scientific Quality	(8) Considered Quality in Report	(9) Methods to Combine Appropriate	(10) Assessed Publication Bias	(11) Stated Conflict of Interest
Abdulkarim et al, 2013 (5)	8	✓	✓		✓		✓	✓		✓	✓	✓
Pakvis et al, 2011 (6)	7	✓		✓			✓	✓	✓	✓		✓
Toossi et al, 2013 (7)	7	✓	✓	✓	✓			✓		✓		✓
Voigt et al, 2012 (8)	9	✓	✓	✓	✓	✓		✓		✓	✓	✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews.
[a]Maximum possible score is 11. Details of AMSTAR score are described in Shea et al. (3)

Table A2: GRADE Evidence Profile for Comparison of Cemented and Uncemented Fixation for Primary Hip Arthroplasty

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Revisions							
6 (RCTs)	Serious limitations (–1)[a]	No serious limitations	No serious limitations	Serious limitations (–1)[b]	Undetected	None	⊕⊕ Low

Abbreviations: RCT, randomized controlled trial.
[a]Studies had limits with respect to allocation concealment and blinding, but because the nature of the outcome was nonsubjective, there was less risk that these biases would influence the outcome of interest. Therefore, this risk of bias was deemed a serious limitation. Details on risk of bias are described in Table A3.
[b]The confidence interval around the pooled effect estimate was wide enough to cross the clinical decision threshold between recommending and not recommending treatment.

Table A3: Risk of Bias Among Randomized Controlled Trials for Comparison of Cemented and Uncemented Fixation for Primary Hip Arthroplasty

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Kärrholm et al, 1994 (9)	Limitations[a]	Limitations[b]	Limitations[c]	No limitations	No limitations
Laupacis et al, 2002 (10)	Limitations[d]	No limitations	Limitations[c]	No limitations	No limitations
Önsten et al, 1994 (11)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Reigstad et al, 1993 (12)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Ström et al, 2006 (13)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Wykman et al, 1991 (14)	Limitations[a]	Limitations[b]	No limitations	No limitations	Limitations[e]

[a]Insufficient details were provided to ensure allocation concealment was present.
[b]Patients were not blinded to treatment arm.
[c]Analysis was per-protocol, as opposed to intention-to-treat; results may therefore contain bias, because the outcomes of patients lost to follow-up were uncertain.
[d]Assessors of outcomes were blinded, but surgeons were not.
[e]Randomization was not truly random; consecutive assignment to study groups was applied.

References

(1) Canadian Institute for Health Information. Hip and knee replacements in Canada: Canadian Joint Replacement Registry 2013 annual report. Ottawa (ON): CIHI; 2013. 94 p.

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(11) Onsten I, Carlsson AS. Cemented versus uncemented socket in hip arthroplasty. A radiostereometric study of 60 randomized hips followed for 2 years. Acta Orthop Scand. 1994 Oct;65(5):517-21.

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Antibiotic-Laden Bone Cement for Primary Knee Arthroplasty: A Rapid Review

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

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In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

ALBC	Antibiotic-laden bone cement
AMSTAR	Assessment of Multiple Systematic Reviews
CADTH	Canadian Agency for Drugs and Technologies in Health
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HTIS	Health Technology Inquiry Service
IV	Intravenous
No.	Number
OA	Osteoarthritis
Op	Operative
OR	Odds ratio
RA	Rheumatoid arthritis
RCT	Randomized controlled trial
TKA	Total knee arthroplasty

Background

Objective of Analysis

This rapid review aimed to determine the safety and effectiveness of antibiotic-laden bone cement (ALBC) versus plain bone cement for primary knee arthroplasty.

Clinical Need and Target Population

Deep infection is a serious and potentially devastating complication of knee arthroplasty. The rate of infection after primary knee arthroplasty is estimated to be between 0.5% and 2%, with the incidence rising as the total number of primary knee arthroplasties increases. (1)

Prophylactic use of ALBC in addition to intravenous antibiotic for primary arthroplasty has been suggested to reduce the risk of infection. (2-4) The ALBC is believed to release antibiotic locally to the surrounding knee tissues, thus establishing resistance to bacterial organisms that could cause infection after joint replacement. Commercially available low-dose ALBC contains less than 1 g of antibiotic per 40 g of cement. (1;5) The effectiveness of ALBC in reducing the rate of deep infections for primary knee arthroplasty, however, remains unclear.

Rapid Review

Research Question

What is the safety and effectiveness of antibiotic-laden bone cement (ALBC) in comparison with plain bone cement for patients undergoing primary knee arthroplasty?

Research Methods

Literature Search

A literature search was performed on April 22, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2005, until April 22, 2013. Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2005, and April 22, 2013
- systematic reviews, meta-analyses, and health technology assessments
- primary knee arthroplasty population
- comparison of ALBC to plain bone cement

Exclusion Criteria

- studies where discrete results for outcomes of interest cannot be abstracted
- evaluation of use of ALBC for revision knee arthroplasty

Outcomes of Interest

- infections
- revisions

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. The panel was composed of physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from the community.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to place into context the evidence produced by Health Quality Ontario and to provide advice on the appropriate clinical pathway for hip and knee arthroplasty in Ontario's health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was used to assess the quality of the final selection of systematic reviews. (6) Primary studies were abstracted from the selected reviews and referenced for assessment of the 2 outcomes of interest.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group criteria. (7) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural method.

Study design was the first consideration; the starting assumption was that randomized controlled trials are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that can raise the quality of evidence were considered: large magnitude of effect, dose-response gradient, and accounting for all residual confounding factors. (7) For more detailed information, please refer to the latest series of GRADE articles. (7)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Literature Search

The database search yielded 192 citations published between January 1, 2005, and April 5, 2013 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One systematic review and a Health Technology Inquiry Service (HTIS) report by the Canadian Agency for Drugs and Technologies in Health (CADTH) were identified that included studies evaluating the use of ALBC for knee arthroplasty. (1;8) Reference lists of the studies included in the reviews as well as health technology assessment websites were further hand-searched, and an updated CADTH review was identified. (9) The updated CADTH HTIS report was not considered a formal systematic review, and therefore was used only as a reference source.

Summary of Included Reviews

The identified systematic reviews and health technology assessment reports are summarized in Table 1. (1;8;9) The methodologic quality of both reviews was poor, with AMSTAR ratings ranging from 4 to 5 of a possible 11 (see Appendix 2; Table A1).

Table 1: Systematic Reviews Evaluating Antibiotic-Laden Bone Cement for Knee Arthroplasty

Author, Year	Search Strategy Dates	Population Included in Review	Number of Studies Related to Primary Knee Arthroplasty	AMSTAR Rating
Block and Stubbs, 2005 (8)	1965–2003 (all study types)	Primary joint arthroplasty	2 RCTs	4
CADTH, 2008 and 2010 update (1;9)	2003–2008 (all study types) Update: 2008–2010	Orthopedic surgeries (primary and revisions)	Review by Block and Stubbs and 2 observational studies	5

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; CADTH, Canadian Agency for Drugs and Technologies in Health; RCT, randomized controlled trial.

The identified reviews and health technology assessment reports included broad search strategies evaluating all joint replacements; however, no analyses were specific to knee arthroplasty. References for individual studies specifically stated by the reviews as evaluating the use of ALBC in primary knee arthroplasty were therefore extracted and analyzed for the current rapid analysis, identifying 2 RCTs and 2 observational studies. Upon further review of the identified studies, 1 observational study was excluded, as few patients in the comparator group did not receive cement (confirmed by personal communication with primary author). (10) The remaining individual studies extracted are summarized in Table 2. (11–13)

Table 2: Studies of Primary Knee Arthroplasty Included in Systematic Reviews

Author, Year	Study Type (Years)	Country	Population	Exclusion Criteria	Intervention (ALBC)	Comparator (Plain Bone Cement)	Additional Antibiotics Received
Chiu et al, 2002 (11)	RCT (1993–1998)	Taiwan	Primary TKA	Diabetes, peripheral arterial occlusive disease, psoriasis, prior knee surgery, lower-extremity infection, osteomyelitis, malignant tumour, or current immunosuppressive treatment	Cefuroxime in Simplex P cement	Simplex P cement	IV cefazolin and gentamicin pre-op and post-op; oral cefazolin 7 d
Chiu et al, 2001 (12)	RCT (1994–1998)	Taiwan	Primary TKA with diabetes and OA	RA, psoriasis, previous knee surgery, infection of the lower limb, osteomyelitis, malignant tumour, or undergoing immunosuppressive treatment	Cefuroxime in Simplex P cement	Simplex P cement	IV cefazolin and gentamicin pre-op and post-op; oral cefazolin 7 d
Gandhi et al, 2009 (13)	Observational with contemporaneous controls (1998–2006)	Canada	Primary TKA with OA or RA	Prior knee sepsis	Simplex T cement (trobramycin impregnated)	Simplex P cement	1 dose systemic antibiotics pre-op and for 24 h after surgery

Abbreviations: ALBC, antibiotic-laden bone cement; IV, intravenous; OA, osteoarthritis; op, operative; RA, rheumatoid arthritis; RCT, randomized controlled trial; TKA, total knee arthroplasty.

Results for Outcomes of Interest

Infections

All 3 of the included studies evaluated deep infections as the primary outcome of interest. None of the included studies evaluated the effect of ALBC on revision surgeries. Results are summarized in Table 3. (11-13)

Table 3: Risk of Deep Infection after Primary Total Knee Arthroplasty for Patients Receiving Antibiotic-Laden Bone Cement versus Plain Bone Cement

Author, Year	Study Type	Mean Length of Follow-up (range)	Deep Infection N (%)		Statistical Significance of Risk of Infection with ALBC versus Plain Bone Cement
			ALBC	Plain Bone Cement	
Chiu et al, 2002 (11)	RCT	49 mo (26–80)	0/178 (0%)	5/162 (3.1%)	*P* = 0.024
Chiu et al, 2001 (12)	RCT	50 mo (26–88)	0/41 (0%)	5/37 (13.5%)	*P* = 0.021
Gandhi et al, 2009 (13)	Observational	1 y	18/814 (2.2%)	25/811 (3.1%)	Unadjusted: *P* = 0.27 Adjusted[a] OR (95% CI): 1.1 (0.4, 3.1); *P* = 0.85

Abbreviations: ALBC, antibiotic-laden bone cement; CI, confidence interval; OR, odds ratio; RCT, randomized controlled trial.
[a]Multivariate linear regression model including age, sex, body mass index, Charlson Index, education, diagnosis of rheumatoid arthritis, and preoperative Western Ontario and McMaster Universities Arthritis Index score.

Randomized Controlled Trials

Chiu et al found a decrease in the rate of deep infection among patients with diabetes and osteoarthritis receiving cefuroxime-laden bone cement in comparison with plain bone cement (*P* = 0.02) (11) as well as among patients without diabetes (*P* = 0.02). (12) These studies might not be generalizable to Ontario, as the authors self-identified as having poor operating room environments. The GRADE for this body of evidence was assessed as very low (See Appendix 2, Tables A2 and A3). (11;12)

Observational Studies

Gandhi et al. (13) found no significant difference in the rate of deep infection between patients who received tobramycin-laden bone cement and those who received plain bone cement (*P* = 0.27). The use of ALBC was not found to be predictive of infection at 1 year in an adjusted analysis (*P* = 0.84). The GRADE for this body of evidence was assessed as very low (See Appendix 2, Tables A2 and A3). (13)

Conclusions

- Based on very low quality evidence, 2 randomized controlled trials identified significantly lower infection rates with antibiotic-laden bone cement (ALBC) versus plain bone cement among patients with and without diabetes receiving primary total knee arthroplasty.

- Based on very low quality of evidence, 1 observational study found no significant difference between patients receiving ALBC versus plain bone cement for primary knee arthroplasty.

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Expert Panel for Health Quality Ontario: Episode of Care for Primary Hip/Knee Replacement

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Orthopaedic Surgery		
Dr John Rudan	Queens University Kingston General Hospital	Head of Department of Surgery Orthopaedic Surgeon
Dr Jeffrey Gollish	Sunnybrook Health Sciences Centre University of Toronto	Medical Director of the Holland Orthopaedic & Arthritic Centre Associate Professor, Division of Orthopaedic Surgery
Dr Maurice Bent	North York General Hospital	Chief, Division Orthopedic Surgery
Dr David Backstein	Mount Sinai Hospital University of Toronto	Division Head of Orthopaedic Surgery Associate Professor
Dr Paul E. Beaulé	University of Ottawa	Professor of Surgery, Head of Adult Reconstruction
Dr Steven MacDonald	London Health Science Centre University of Western Ontario	Site Chief of Orthopaedic Surgery Professor, Division of Orthopaedic Surgery
Dr Mitchell Winemaker	Hamilton Health Sciences – Chief of Orthopedic Surgery	Juravinski Hospital McMaster University Associate Professor
Dr Andrew Van Houwellingen	Orthopaedic Surgeon	St. Thomas Elgin General Hospital
Primary Care		
Dr Tatiana Jevremovic	University of Western Ontario Fowler Kennedy Sport Medicine Clinic	Assistant Professor Department of Family Medicine
Dr Christopher Jyu	Rouge Valley Health System The Scarborough Hospital	Primary Care Lead

Panel Member	Affiliation(s)	Appointment(s)
Internal Medicine		
Dr Valerie Palda	St. Michael's Hospital University of Toronto	General Internist Associate Professor, Department of Medicine
Anesthesiology		
Dr Nick Lo	St. Michael's Hospital University of Toronto	Staff Anesthesiologist Assistant Professor, Department of Anesthesiology
Dr Colin McCartney	Sunnybrook Health Sciences Centre University of Toronto	Staff Anesthesiologist Associate Professor
Geriatric Medicine		
Dr Anna Byszewski	The Ottawa Hospital Regional Geriatric Program of Eastern Ontario	Staff Geriatrician Full Professor, University of Ottawa
Physiotherapy and Rehabilitation		
Caroline Fanti	Thunder Bay Regional Health Sciences Centre	Physiotherapist
Deborah Marie Kennedy	Sunnybrook Holland Orthopaedic and Arthritic Centre	Manager, Rehabilitation and MSK Program Development
Raymond Kao	St. Michael's Hospital	Case Manager, Inpatient Mobility Program
Dr Peter Nord	Providence Healthcare Foundation University of Toronto	Vice President, Chief Medical Officer and Chief of Staff
Executive Administration		
Anne Marie MacLeod	Sunnybrook Health Science Centre	Operations Director
Tiziana Silveri	North Bay Regional Health Centre	Vice President, Clinical Services
Rhona McGlasson	Bone and Joint Canada	Executive Director
Brenda Flaherty	Hamilton Health Sciences	EVP and Chief Operating Officer
Charissa Levy	GTA Rehab Network	Executive Director
Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

Appendices

Appendix 1: Literature Search Strategies

Literature Search—Hip and Knee Arthroplasty QBP Rapid Review—Knee Bone Cement

Search date: April 22, 2013
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase; Cochrane Library; Centre for Reviews and Dissemination
Limits: 2005-current; English
Filters: none

Database: Embase 1980 to 2013 Week 16, Ovid MEDLINE(R) 1946 to April Week 2 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 19, 2013
Search Strategy:

#	Searches	Results
1	exp Arthroplasty, Replacement, Knee/ use mesz or Arthroplasty, Replacement/ use mesz	14761
2	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	32542
3	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	47575
4	or/1-3	51222
5	exp Bone Cements/ use mesz	16497
6	exp Bone Cement/ use emez	10145
7	((bone* or orthop?edic*) adj2 (paste* or glue* or cement*)).ti,ab.	11267
8	or/5-7	30789
9	exp Anti-Bacterial Agents/ use mesz or exp Anti-Infective Agents/ use mesz	1195043
10	exp antibiotic agent/ use emez or exp antiinfective agent/ use emez	2005786
11	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetroprim).ti,ab.	654735
12	exp antibiotic bone cement/ use emez	17
13	or/9-12	3383241
14	4 and 8 and 13	461
15	limit 14 to english language	416
16	limit 15 to yr="2005 -Current"	255
17	remove duplicates from 16	190

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees	1279
#2	MeSH descriptor: [Arthroplasty, Replacement] explode all trees	2541
#3	MeSH descriptor: [Knee Prosthesis] explode all trees	501
#4	((knee* near/2 (replacement* or arthroplast*)) or (knee* near/2 prosthes?s) or TKR):ti,ab,kw (Word variations have been searched)	2211
#5	#1 or #2 or #3 or #4	3444
#6	MeSH descriptor: [Bone Cements] explode all trees	274
#7	((bone* or orthop?edic*) near/2 (paste* or glue* or cement*)):ti (Word variations have been searched)	70
#8	((bone* or orthop?edic*) near/2 (paste* or glue* or cement*)):ab (Word variations have been searched)	150
#9	#6 or #7 or #8	348
#10	MeSH descriptor: [Anti-Bacterial Agents] explode all trees	8281
#11	MeSH descriptor: [Anti-Infective Agents] explode all trees	21040
#12	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetroprim):ti (Word variations have been searched)	3806
#13	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetroprim):ab (Word variations have been searched)	4450
#14	#10 or #11 or #12 or #13	25162
#15	#5 and #9 and #14 from 2005 to 2013	5

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR Arthroplasty, Replacement, Knee EXPLODE ALL TREES	242
2	MeSH DESCRIPTOR Arthroplasty, Replacement	46
3	MeSH DESCRIPTOR Knee Prosthesis EXPLODE ALL TREES	60
4	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR)	431
5	#1 OR #2 OR #3 OR #4	489
6	MeSH DESCRIPTOR Bone Cements EXPLODE ALL TREES	45
7	((bone* or orthop?edic*) adj2 (paste* or glue* or cement*))	69
8	#6 OR #7	69
9	MeSH DESCRIPTOR Anti-Bacterial Agents EXPLODE ALL TREES	1016
10	MeSH DESCRIPTOR Anti-Infective Agents EXPLODE ALL TREES	2229
11	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetroprim)	583
12	#9 OR #10 OR #11	2522
13	#5 AND #8 AND #12	3
14	(#13) FROM 2005 TO 2013	2

Appendix 2: Quality Assessment Tables

Table A4: Assessment of Multiple Systematic Reviews (AMSTAR) Score of Reviews

Author, Year	AMSTAR Score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
CADTH, 2008 (1)	5			✓	✓	✓	✓					✓
Block and Stubbs, 2005 (8)	4	✓						✓	✓			✓

Abbreviations: AMSTAR, assessment of multiple systematic reviews; CADTH, Canadian Agency for Drugs and Technologies in Health.
[a]Details of AMSTAR method are described in Shea et al. (6)

Table A2: GRADE Evidence Profile for Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Infections							
2 (RCTs)	Very serious limitations (−2)[a]	No serious limitations	Serious limitations (−1)[b]	No serious limitations[c]	Undetected	None	⊕ Very low
1 (observational)	Very serious limitations (−2)[d]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low

Abbreviations: No., number; RCT, randomized controlled trial.
[a]See Appendix 2, Table A3 for Risk of Bias table.
[b]Operating room standards in both studies might not reflect practices in Ontario. Authors described their operating room environments as poor and their patients as in a poor state of hygiene. Operations were performed in operating theatres without routine ultraviolet lights for disinfection, laminar flow, special air handling, or isolation suits.
[c]No power calculation was provided by the authors. Similarly, no effect estimate or confidence intervals were provided by the authors.
[d]See Appendix 2, Table A4 for Risk of Bias table.

Table A3: Risk of Bias Among Randomized Controlled Trials for the Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Chiu et al, 2002 (11)	Serious limitations[a]	Serious limitations[b]	Serious limitations[c]	No limitations	Serious limitations[d]
Chiu et al, 2001 (12)	Serous limitations[a]	Serious limitations[b]	Serious limitations[c]	No limitations	Serious limitations[d]

[a]Quasi-randomized study design, patients randomized by odd and even chart numbers.
[b]Physicians were not blinded, and it was not stated if the patient or outcome assessors were blinded.
[c]It was not stated how long patients were followed up, or who was lost to follow-up. Average duration of follow-up ranged from 26 to 80 months.
[d]Bilateral total knee replacements were randomized by patient leg.

Table A4: Risk of Bias Among Observational Trials for the Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
Gandhi et al, 2009 (13)	Serious limitations[a]	No limitations	No limitations	Serious limitations[b]	No limitations

[a]How patients were assigned to the surgeon, and how selection of procedure was determined by the surgeon was unclear.
[b]There was no assessment of individual comorbidities that can increase risk of infection; only Carlson Index was included in adjusted analysis.

References

(1) Murphy G, Spry C, Canadian Agency for Drugs and Technologies in Health, Health Technology Inquiry Service. Antibiotic infused bone cement for orthopedic surgeries: a review of the clinical benefit and harm [Internet]. Canada; 2008. Available from: http://www.cadth.ca/media/pdf/htis/L0040%20Antibiotic%20Infused%20Bone%20Cement%20for%20Orthopedic%20Surgeries%20final.pdf.

(2) British Orthopaedic Association. Primary total hip replacement: a guide to good practice. London, England: 2012 38p. Available from: http://www.britishhipsociety.com/uploaded/Blue%20Book%202012%20fsh%20nov%202012.pdf.

(3) British Orthopeaedic Association. Knee replacement: a guide to good practice [Internet]. London, England; 1999. 24p. Available from: http://www.boa.ac.uk/Publications/Documents/tkr_good_practice.pdf.

(4) Scottish Intercollegiate Guidelines Network (SIGN). Antibiotic prophylaxis in surgery: a national clinical guideline [Internet]. London, England; 2008. 71p. Available from: http://www.sign.ac.uk/pdf/sign104.pdf.

(5) Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. J Bone Joint Surg. 2006;88(11):2487-500.

(6) Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7(10):1-7.

(7) Guyatt GH, Oxman AD, Schunemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr; 64(4):380-2.

(8) Block JE, Stubbs HA. Reducing the risk of deep wound infection in primary joint arthroplasty with antibiotic bone cement. Orthopedics. 2005;28(11):1334-45.

(9) Canadian Agency for Drugs and Technologies in Health,Health Technology Inquiry Service. Antibiotic infused bone cement for orthopedic surgeries: clinical and cost-effectiveness. [Internet]. 2010 5p. Available from: http://www.cadth.ca/media/pdf/K0146_Antibiotic-Infused_Bone_Cement_final.pdf.

(10) Namba RS, Chen Y, Paxton EW, Slipchenko T, Fithian DC. Outcomes of routine use of antibiotic-loaded cement in primary total knee arthroplasty. J Arthroplast. 2009;24(6 Suppl):44-7.

(11) Chiu FY, Chen CM, Lin CFJ, Lo WH. Cefuroximine-impregnated cement in primary total knee arthroplasty: a prospective, randomized study of three hundred and forty knees. J Bone Joint Surg. 2002;84-A(5):759-62.

(12) Chiu FY, Lin CFJ, Chen CM, Lo WH, Chaung TY. Cefuroximine-impregnated cement at primary total knee arthroplasty in diabetes mellitus. J Bone Joint Surg (Br). 2001;83-B(5):691-5.

(13) Gandhi R, Razak F, Pathy R, Davey JR, Syed K, Mahomed NN. Antibiotic bone cement and the incidence of deep infection after total knee arthroplasty. J Arthroplast. 2009;24(7):1015-8.

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Local Infiltration Analgesia in Hip and Knee Arthroplasty: A Rapid Review

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Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

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In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature search specified in the Research Methods section, as appropriate. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
LIA	Local infiltration analgesia
RCT	Randomized controlled trial
THA	Total hip arthroplasty
TKA	Total knee arthroplasty

Background

Objective of Analysis

The objective of this rapid review was to examine the effectiveness of local infiltration analgesia in patients who have undergone primary hip arthroplasty or primary knee arthroplasty.

Clinical Need and Target Population

Primary hip or knee arthroplasty surgery requires appropriate anesthesia and analgesia to minimize patient discomfort and promote recovery. Multimodal pain management strategies are common and may include a combination of analgesics, such as opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), and/or regional anesthetics, such as epidurals and femoral nerve blocks. (1-3) Pain management medications for patients undergoing total knee arthroplasty (TKA) or total hip arthroplasty (THA) can be administered through a number of different modalities such as oral, local injection, or epidural injection. (4) Local infiltration analgesia (LIA) is one such modality of pain management administered as a "cocktail" of a combination of many pain medications into the intra-articular space of the joints or other tissues at the site of the joint. The cocktail may be administered directly or through a catheter. (5) What remains uncertain, however, is if LIA provides superior pain management compared with other pain management strategies.

Rapid Review

Research Question

What is the effectiveness of local infiltration analgesia (LIA) in primary hip arthroplasty and primary knee arthroplasty?

Research Methods

Literature Search

Search Strategy

A literature search was performed on May 16, 2013, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews for studies published from January 1, 2008, until May 16, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-text publications
- published between January 1, 2008, and May 16, 2013
- systematic reviews, meta-analyses, and health technology assessments
- primary hip arthroplasty or primary knee arthroplasty
- local infiltration analgesia at the surgical joint site

Exclusion Criteria

- studies from which results on outcomes of interest cannot be abstracted

Outcomes of Interest

- pain
- hospital length of stay

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community laboratories.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for a hip and knee arthroplasty in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool is used to assess the methodological quality of the final selection of systematic reviews. (6) Primary studies were abstracted from the selected reviews and referenced for quality assessment of the body of the evidence for the 2 outcomes of interest.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (7) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (7) For more detailed information, please refer to the latest series of GRADE articles. (7)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 349 citations published between January 1, 2008, and May 16, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Four systematic reviews met the inclusion criteria. The reference lists of the included studies, health technology assessment websites, and other resources were hand searched to identify other relevant studies, and no additional citations were identified.

Quality Assessment of Reviews

The included reviews are summarized in Table 1 below. The AMSTAR scores of the identified reviews, ranged from 1 to 8 out of a possible 11. (6) Only 3 of the reviews specifically examined LIA in patients undergoing TKA or THA. (5;8;9) The other review examined pain management in the target population more broadly and included local infiltration as one of the pain management strategies reviewed. (4)

Table 1: Summary of Included Reviews

Author, Year	Search Dates	Study Designs Included	Population	Objective of Review	AMSTAR[a]
Fischer et al, 2008 (4)	1966–2005	RCT	TKA	An examination of various analgesics	8
Gibbs et al, 2012 (8)	Not reported	RCT and observational	TKA	An examination of local administration analgesics	1
McCarthy & Iohom, 2012 (9)	1966–2012	RCT and observational	THA	An examination of intraoperative local anesthetic infiltration for pain management postoperatively	5
Starks et al, 2011 (5)	Not reported	RCT	TKA and THA	An examination of the role of local anesthetics in joint replacement surgery	1

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty.
[a] Out of a possible 11, with higher scores representing higher methodological quality; details of scores are shown in Appendix 2, Table A1.

The low AMSTAR scores indicate a number of methodological flaws in the Gibbs et al (8) and Starks et al (5) reviews, and for this reason these 2 reviews were excluded from this rapid review and were only used as additional references for supplementary details on the primary studies. As a result, the Fischer et al (4) review of LIA in patients undergoing total knee arthroplasty (TKA) and the McCarthy and Iohom (9) review of LIA in patients undergoing total hip arthroplasty (THA) were included.

Summary of Included Reviews

The Fischer et al (4) review identified 112 studies, of which 74 studies evaluated pharmacological mechanisms of pain management; of these, 8 randomized controlled trails (RCTs) examined LIA. (4) The review by McCarthy and Iohom (9) included 8 RCTs and 2 observational studies.

The Fischer et al (4) and McCarthy and Iohom (9) reviews concluded that intra-articular analgesic techniques are not recommended due to the inconsistency of the results, and that, while there are some advantages when compared to placebo, there is no additive benefit when combined with a multimodal analgesic approach.

Infiltration Cocktails of Included Primary Studies

There were a number of differences in the intervention and control protocols in the primary studies included in the Fischer et al (4) and McCarthy and Iohom (9) reviews. Some of the differences included variations in the timing and method of administration of the LIA (before/during/after closure of the surgical wound; with or without a catheter); variations in the control group (other analgesics, saline combined with other analgesics, saline alone with postoperative analgesics only or no control); and variations in the LIA cocktails (see Table 2).

Table 2: Summary of Interventions in the Included Primary Studies

Author, Year	Intervention (LIA cocktail)[a]	Control
TKA population		
Badner et al, 1996 (10)	150 mg bupivacaine 0.15 mg epinephrine	Saline
Badner et al, 1997 (11)	150 mg bupivacaine 1.5 mg adrenaline 1 mg morphine	Saline
Browne et al, 2004 (12)	100 mg bupivacaine	Saline
Klasen et al, 1999 (13)	1 mg morphine	No local infiltration
Mauerhan et al, 1997 (14)	50 mg bupivacaine 5 mg morphine	Saline
Nechleba et al, 2005 (15)	100 mg bupivacaine Plus bolus of 10.25 mg bupivacaine per hour	Saline
Ritter et al, 1999 (16)	10 mg morphine 25 mg bupivacaine	Saline
Tanaka et al, 2001 (17)	75 mg bupivacaine 0.15 mg epinephrine 5 mg morphine	Saline and epinephrine
THA population		
Andersen et al, 2007 (18)	200 mg ropivacaine 0.5 mg epinephrine 30 mg ketorolac Plus bolus at 8 hours of 20 mL of 150 mg ropivacaine, 0.5 mg epinephrine, and 30 mg ketorolac	Epidural to 20 hours
Andersen et al, 2007 (19)	300 mg ropivacaine 30 mg ketorolac 0.5 mg epinephrine Plus bolus in the morning of 20 mL of the cocktail	Saline
Andersen et al, 2011 (20)	340 mg ropivacaine 1.7 mg epinephrine	Saline
Bianconi et al, 2003 (21)	200 mg ropivacaine Plus extra-articular infusion ropivacaine 10 mg per hour for 55 hours	Extra-articular saline infusion
Busch et al, 2010 (22)	400 mg ropivacaine 0.6 mg epinephrine 30 mg ketorolac 5 mg morphine	No local infusion

Kerr & Lohan, 2008 (23)	300 mg ropivacaine 1.5 mg epinephrine 30 mg ketorolac Plus bolus at 15–20 hours of 50 mL of the cocktail	No control group
Lunn et al, 2011 (24)	300 mg ropivacaine 1.5 mg epinephrine Plus a multimodal analgesic management of pain	Saline and a multimodal analgesic management of pain
Otte et al, 2008 (25)	300 mg ropivacaine 1.5 mg epinephrine	No control group
Parvateneni et al, 2007 (26)	200–400 mg bupivacaine 4–10 mg morphine 0.3 mg epinephrine 40 mg methylprednisolone 750 mg cefuroxime	No local infusion
Specht et al, 2011 (27)	200 mg ropivacaine 30 mL ketorolac 1 mg epinephrine Plus bolus of 51 mL with IA catheter at 10 and 22 hours of the cocktail and a multimodal analgesic management of pain	Saline and a multimodal analgesic management of pain

Abbreviations: IA, intra-articular; LIA, local infiltration analgesia; THA, total hip arthroplasty; TKA, total knee arthroplasty.
[a] The details of the interventions were pulled from the Fischer et al (4), Gibbs et al (8), McCarthy & Iohom (9), and Starks et al (5) reviews and were further supplemented by the individual primary studies only on an as-needed basis.

Results for the Outcomes of Interest

Pain

All of the individual studies included in the two reviews reported pain as an outcome measure, but neither review conducted a meta-analysis or other quantitative summary of the results for this outcome. Table 3 shows a summary from the reviews of the results for the outcome of pain.

Table 3: Summary of Results for Pain

Author, Year	Population	Intervention/ Comparator	Included Studies	Results	GRADE
Fischer et al, 2008 (4)	TKA	Intra-articular LIA / placebo or no treatment	8 RCTs	Mixed results Significant decrease in pain in 2 studies; no statistically significant difference in 5 studies; inconclusive results in 1 study	Very low
McCarthy & Iohom, 2012 (9)	THA	LIA/ placebo or usual care or no comparator	8 RCTs; 2 observational studies	Mixed results Significant decrease in pain in 8 studies; no statistically significant difference in 2 studies	Very low

Abbreviations: LIA, local infiltration analgesia; RCT, randomized controlled trail; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Overall, the results for the effectiveness of LIA to manage pain were inconsistent. This result was based on very low quality of evidence (Appendix 2, Table A2).

Hospital Length of Stay

Only the McCarthy and Iohom review (9) examined hospital length of stay as an outcome measure. A summary of the results is described in Table 4.

Table 4: Summary of Results for Length of Stay

Author, Year	Population	Intervention/ Comparator	Included Studies	Results	GRADE
McCarthy & Iohom, 2012 (9)	THA	LIA / placebo or usual care or no treatment	5 RCTs	Mixed results Significant ↓in LOS in 3 studies; no statistically significant difference in 2 studies	Very low

Abbreviations: LIA, local infiltration analgesia; LOS, length of stay; RCT, randomized controlled trial; THA, total hip arthroplasty.

Overall, the results for the impact of LIA on hospital length of stay were inconsistent. This result was based on very low quality of evidence (Appendix 2, Table A2).

Conclusions

Based on very low quality of evidence:

- The results for the impact of local infiltration analgesia on pain in patients undergoing either total hip or knee arthroplasty were inconsistent.
- The results for the impact of local infiltration analgesia on hospital length of stay in patients undergoing total hip arthroplasty, based on very low quality of evidence, were inconsistent.

Acknowledgements

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Expert Panel for Health Quality Ontario: Episodes of Care for Primary Hip/Knee Replacement

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Jane DeLacy	William Osler Health System	Executive Director Clinical Services
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Appendices

Appendix 1: Literature Search Strategies

Search date: May 16, 2013
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; All EBM Reviews

#	Searches	Results
1	exp Arthroplasty, Replacement, Hip/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	20435
2	exp hip arthroplasty/ use emez or exp Hip Prosthesis/	55638
3	((hip* adj2 (replacement* or arthroplast*)) or ((femoral head* or hip*) adj2 prosthes?s) or THR).mp.	115083
4	or/1-3	119434
5	exp Arthroplasty, Replacement, Knee/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	16304
6	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	33189
7	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	50406
8	or/5-7	54230
9	4 or 8	158633
10	exp Analgesia/	131354
11	exp Analgesics/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	452034
12	exp analgesic agent/ use emez	596408
13	exp Anesthesia/	412137
14	exp anesthetic agent/ use emez	204605
15	exp Anesthetics/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	219860
16	or/10-13	1426782
17	(infiltra* or instill* or infus* or lia).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	983304
18	16 and 17	87227
19	((Intraarticular or knee* or hip? or intra-articular or periarticular or peri-articular or wound* or joint*) adj2 (injection* or infiltat* or infus* or instill*)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	18114
20	((infiltra* or instill* or infus*) adj2 (analgesi* or an?esthesia*or ropivacaine or ketorolac or adrenaline or steroid* or magnesium sulphate or morphine or nonsteroidal anti-inflammatory or nsaid* or opiod* or anti-hyperalgesic* or pregabalin or s-ketamine or epinephrine or bupivacaine)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	15585
21	lia.mp.	1474
22	19 or 20 or 21	34538
23	18 or 22	111906
24	9 and 23	2053
25	limit 24 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	997
26	remove duplicates from 25	691
27	(Meta Analysis or Controlled Clinical Trial or Randomized Controlled Trial).pt.	867226
28	Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	49681
29	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	82162
30	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane or ((health technolog* or biomedical technolog*) adj2 assess*)).ti,ab.	354090
31	exp Random Allocation/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Double-Blind Method/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Control Groups/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Placebos/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	331119
32	Randomized Controlled Trial/ use emez or exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	613192
33	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2090938
34	exp Standard of Care/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Guideline/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Guidelines as Topic/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	130082
35	exp Practice Guideline/ use emez or exp Professional Standard/ use emez	545615
36	(guideline* or guidance or consensus statement* or standard or standards).ti.	234585
37	or/27-36	3641482
38	26 and 37	352

Appendix 2: Quality Assessment Tables

Table A1: AMSTAR score of Reviews[a]

Author, Year	AMSTAR score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
Fischer et al, 2008 (4)	8	✓		✓		✓	✓	✓	✓	✓		✓
Gibbs et al, 2012 (8)	1						✓					
McCarthy & Iohom, 2012 (9)	5	✓		✓			✓	✓	✓			
Starks, 2011 (5)	1						✓					

[a] Details of AMSTAR method are described in Shea et al. (6)

Table A2: GRADE Evidence Profile for Local Infiltration Analgesia in Primary Hip and Knee Arthroplasty

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Pain in TKA population							
8 (RCTs)	No serious limitations[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[d]	Undetected	None	⊕ Very Low
Pain in THA population							
8 (RCTs)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[e]	Undetected	None	⊕ Very Low
2 (observational)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[e]	Undetected	None	⊕ Very Low
Length of Stay in THA population							
5 (RCTs)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[f]	Undetected	None	⊕ Very Low

Abbreviations: RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty

[a] For details about risk of bias of individual studies see Table A3 and Table A4.

[b] Some studies identified a statistically significant difference while others found no difference or had inconclusive results.

[c] All studies had differences in protocols for the administration of local infiltration analgesics with variations in medication types, dosage, and timing of administration as well as differences in control groups including the use of a placebo, usual care, or no control arm.

[d] No meta-analysis was conducted; using the power calculation provided in the publication by Bianconi et al (21), all study samples were sufficiently large.

[e] No meta-analysis was conducted; using the power calculation provided in the publication by Bianconi et al (21), all but 2 of the study samples were sufficiently large.

[f] No meta-analysis was conducted; appropriate power calculation for outcome of length of stay is unknown.

Table A3: Risk of Bias Among Randomized Controlled Trials for the Examination of Local Infiltration Analgesia

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
TKA population					
Badner et al, 1996 (10)	No limitations	No limitations	No limitations	No limitations	None
Badner et al, 1997 (11)	No limitations	No limitations	No limitations	No limitations	None
Browne et al, 2004 (12)	No limitations	No limitations	No limitations	No limitations	None
Klasen et al, 1999 (13)	Limitations[a]	Limitations[b]	Limitations[c]	No limitations	None
Mauerhan et al, 1997 (14)	No limitations	No limitations	No limitations	No limitations	None
Nechleba et al, 2005 (15)	No limitations	No limitations	No limitations	No limitations	None
Ritter et al, 1999 (16)	No limitations	No limitations	No limitations	No limitations	None
Tanaka et al, 2001 (17)	No limitations	No limitations	No limitations	No limitations	None
THA population					
Andersen et al, 2007 (18)	Limitations[d]	Limitations[b]	Limitations[c]	No limitations	None
Andersen et al, 2007 (19)	No limitations	No limitations	Limitations[c]	No limitations	None
Andersen et al, 2011 (20)	No limitations[e]	No limitations	No limitations	No limitations	None
Bianconi et al, 2003 (21)	Limitations[d]	No limitations	No limitations	No limitations	None
Busch et al, 2010 (22)	Limitations[a]	No limitations	No limitations	No limitations	None
Lunn et al, 2011 (24)	No limitations	No limitations	No limitations	No limitations	None
Parvateneni et al, 2007 (26)	Limitations[a]	Limitations[e]	No limitations	No limitations	None
Specht et al, 2011 (27)	No limitations	No limitations	No limitations	No limitations	None

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.
[a] Surgeons were not blinded though the assessors were.
[b] Patients were not blinded; catheter placement location differed between study groups.
[c] Per protocol analysis, as opposed to intention-to-treat analysis, was conducted.
[d] Surgeons were not blinded.
[e] Patient blinding may be compromised due to differences in the protocols for the various arms of the study.

Table A4: Risk of Bias Among Observational Trials for the Examination of Local Infiltration Analgesia

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
THA population					
Kerr & Lohan, 2008 (23)	Limitations[a]	No limitations	Limitations[b]	Limitations[c]	No limitations
Otte et al, 2008 (25)	No limitations	No limitations	Limitations[b]	Limitations[c]	No limitations

Abbreviations: THA, total hip arthroplasty.
[a] Unclear eligibility criteria.
[b] Patients were not blinded, which may bias the measurement of subjective outcomes such as pain.
[c] Inadequate controlling for potential confounding conducted in analysis.

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Intensity of Rehabilitation During the Acute Hospitalization Period After Hip or Knee Arthroplasty: A Rapid Review

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All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This report was prepared by Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to Health Quality Ontario. It is possible that relevant scientific findings may have been reported since the completion of the review. This report is current to the date of the literature review specified in the methods section, if available. This analysis may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ILOA	Iowa Level of Assistance scale
PT	Physiotherapy
RCT	Randomized controlled trial
SD	Standard deviation
TKA	Total knee arthroplasty
THA	Total hip arthroplasty

Background

Objective of Analysis

The objective of this analysis was to assess the effectiveness of increased intensity of rehabilitation during the acute hospitalization period after primary hip arthroplasty and knee arthroplasty.

Clinical Need and Target Population

Rehabilitation during the immediate postoperative hip or knee arthroplasty period has been recommended to help restore patient mobility, flexibility, and strength and reduce pain prior to discharge. (1-3) Rehabilitation during this period often includes mobilization and weight-bearing activities, which can be delivered by various care providers including physiotherapists (PTs) or occupational therapists. (1-3)

The appropriate intensity of rehabilitation required after hip and knee arthroplasty during the acute hospitalization period remains unclear. For the purpose of this review, rehabilitation intensity was defined as different doses of the same rehabilitation therapy, namely different amounts of time spent in therapy measured either by different lengths of sessions, different number of sessions, or different duration of the overall intervention.

Rapid Review

Research Questions

- What is the effectiveness of higher intensity of rehabilitation compared with lower intensity rehabilitation during the acute hospitalization period after primary hip arthroplasty?
- What is the effectiveness of higher intensity of rehabilitation compared with lower intensity rehabilitation during the acute hospitalization period after primary knee arthroplasty?

Research Methods

Literature Search

Search Strategy

A literature search was performed on May 14, 2013, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews for studies published from January 1, 2008, until May 13, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-text publications
- published between January 1, 2008, and May 13, 2013
- systematic reviews and meta-analyses (if no systematic reviews were identified, randomized controlled trials [RCTs] were included)
- adult primary hip arthroplasty (research question 1) or knee arthroplasty (research question 2) populations
- studies comparing 2 or more doses of intensity (as defined above) of the same type of rehabilitation during the acute postoperative period

Exclusion Criteria

- studies where outcomes of interest cannot be abstracted
- studies that compared 1 dose of therapy with no treatment
- studies that compared 1 dose of therapy with different types of treatment (e.g., weight-bearing exercises versus non-weight-bearing exercises)
- studies that did not describe the control or usual care group intensity

Outcomes of Interest

A maximum of 2 outcomes were assessed, according to the following hierarchical order, as available:

1. Range of motion
2. Functional status
3. Pain
4. Length of stay

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representation from community laboratories.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for a hip and knee arthroplasty in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool is used to assess the methodological quality of systematic reviews. (4)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (5) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that RCTs are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (5) For more detailed information, please refer to the latest series of GRADE articles. (5)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 1,130 citations published between January 1, 2008, and May 13, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Results for Primary Hip Arthroplasty Population (Research Question 1)

The literature search did not identify any systematic reviews or meta-analyses that met the inclusion criteria; as a result, RCTs were included in the search. A single RCT that evaluated the impact of increased intensity of acute care physiotherapy (PT) for patients undergoing total hip arthroplasty (THA) was identified. The reference list of the included study was hand searched to identify any additional potentially relevant studies, but none were identified. A summary of the identified RCT is shown in Table 1.

Table 1: Summary of Randomized Controlled Trial Evaluating Increased Intensity Physiotherapy Rehabilitation During the Acute Hospitalization Period for Total Hip Arthroplasty Patients

Author, Year	Sample Size (Intervention/ Control)	Start Day of Rehabilitation	Intervention (Higher Intensity)	Comparator (Lower Intensity)	Total Extra Minutes of Rehabilitation
Stockton & Mengersen, 2009 (6)	30/27	First day after surgery	2 PT sessions per day	1 PT session per day	Not provided

Abbreviations: PT, physiotherapy.

The RCT evaluated 2 outcomes of interest, functional status and hospital length of stay.

Functional Status

Functional status was assessed by Stockton and Mengersen (6) using the Iowa Level of Assistance Scale (ILOA). The scale ranges from a score of 0 (no assistive device and completely independent) to 50 (using a walking frame but unable to attempt test for safety reasons). (6) A difference of 7 in the scores was considered clinically significant. A summary of the results is shown in Table 2.

Table 2: Functional Status Measured Using Iowa Level of Assistance for Higher Intensity Rehabilitation Compared With Lower Intensity Rehabilitation for Total Hip Arthroplasty

Author, Year	Day of Follow-up	Intervention Mean ILOA (SD)	Control Mean ILOA (SD)	Statistical Significance (*P*)
Stockton & Mengersen, 2009 (6)	3	28.5 (7.6)	32.2 (6.9)	0.041
	6	18.2 (7.7)	20.6 (7.1)	0.129

Abbreviations: ILOA, Iowa Level of Assistance scale; SD, standard deviation.

Overall, there was a statistically significant improvement in ILOA scores at day 3; however, the authors considered this clinically nonsignificant. There was no significant difference in scores at day 6. The GRADE of quality for this body of evidence was assessed as moderate (see Appendix 2, Tables A2 and A4).

Length of Stay

There was no significant difference in mean hospital length of stay between patients receiving twice-a-day PT compared with those receiving once-a-day PT during the immediate acute care phase after THA (Table 3). The GRADE for this body of evidence was assessed as very low (see Appendix 2, Tables A2 and A4).

Table 3: Length of Hospital Stay for Higher Intensity Rehabilitation Compared With Lower Intensity Rehabilitation for Total Hip Arthroplasty

Author, Year	Higher Intensity PT Mean LOS (SD)	Lower Intensity PT Mean LOS (SD)	Statistical Significance (*P*)
Stockton & Mengersen, 2009 (6)	8 (3.3)	8.2 (2.6)	0.851

Abbreviations: LOS, length of hospital stay; PT, physiotherapy; RCT, SD, standard deviation; THA, total hip arthroplasty.

Results for Primary Knee Arthroplasty Population (Research Question 2)

The literature search identified 1 systematic review that evaluated the impact of increased frequency of PT visits on acute care length of stay in patients with total knee arthroplasty (TKA). The reference lists of the included studies and health technology assessment websites were hand searched, and no additional citations were identified. Table 4 provides a summary of the systematic review.

Table 4: Summary of Systematic Review Evaluating Higher Intensity Rehabilitation Compared With Lower Intensity Rehabilitation for Total Knee Arthroplasty

Author, Year	Search Dates	Population Evaluated	Intervention/Comparator Evaluated	Number of Relevant Studies	AMSTAR Score[a]
Kolber et al, 2013 (7)	Unclear; most recent study published in 2011	TKA	1) Twice-daily PT/once-daily PT 2) Weekend visits/Monday through Friday visits	1 RCT	4

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; PT, physiotherapy; RCT, randomized controlled trial; TKA, total knee arthroplasty.

[a] Out of a possible 11, with higher scores representing higher methodological quality; details of scores shown in Appendix 2, Table A1.

Of the 4 studies identified by Kolber et al, (7) only 1 RCT (8) met the inclusion criteria of this rapid review; the remaining studies assessed the impact of weekend visits on hospital length of stay. Given the limited methodological quality of the systematic review (AMSTAR score of 4 out of 11) and no quantitative data provided for the outcome of interest, the individual RCT by Lenssen et al (8) which met the inclusion criteria for the present rapid review, was extracted and assessed.

In their RCT, Lenssen et al (8) evaluated the effectiveness of increased number of PT sessions immediately after surgery for patients undergoing TKA. The intervention consisted of PT twice a day, with patients in the control arm receiving PT once a day. The intervention group received an additional 20 minutes of PT per day. However, how soon after surgery the rehabilitation was started was not mentioned. Because Kolber et al (7) assessed only length of hospital stay as an outcome in their systematic review, only data on this outcome was further extracted from the RCT by Lenssen et al. (8)

Length of Stay

The RCT by Lenssen et al (8) found no significant differences in hospital length of stay for individuals receiving higher intensity acute care PT compared with those receiving lower intensity acute care PT ($P = 0.34$) (Table 5). The GRADE for this body of evidence was assessed as very low.

Table 5. Length of Hospital Stay for Higher Intensity Rehabilitation Compared With Lower Intensity Rehabilitation for Total Knee Arthroplasty

Author, Year	Sample Size (Intervention/ Control)	Higher Intensity PT Mean LOS (SD)	Lower Intensity PT Mean LOS (SD)	Mean Difference in LOS (95% CI)
Lenssen et al, 2006 (8)	21/22	4.1 (0.9)	4.5 (1.3)	0.4 (−0.3, 1.0)

Abbreviations: CI, confidence interval; LOS, length of stay; PT, physiotherapy; SD, standard deviation.

Conclusions

Research Question 1: Intensity of rehabilitation during the acute care stay after primary hip arthroplasty

In total hip arthroplasty (THA) patients receiving higher intensity physiotherapy (PT) rehabilitation compared with lower intensity PT rehabilitation during the immediate acute care hospitalization period, there was

- A statistically, but not clinically, significant difference in functional status measured using the Iowa Level of Assistance score at 3 days after surgery, and no significant difference 6 days after surgery based on ***moderate*** quality of evidence
- No significant difference in acute care hospital length of stay based on ***very low*** quality of evidence

Research Question 2: Intensity of rehabilitation during the acute care stay after primary knee arthroplasty

Among total knee arthroplasty (TKA) patients receiving higher intensity PT rehabilitation compared with lower intensity PT rehabilitation during the immediate acute care hospitalization period, there was no significant difference in hospital length of stay based on ***very low*** quality of evidence.

Acknowledgements

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Expert Panel for Health Quality Ontario: Episode of Care for Primary Hip/Knee Replacement

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Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

Appendices

Appendix 1: Literature Search Strategies

Database: Embase <1980 to 2013 Week 19>, Ovid MEDLINE(R) <1946 to May Week 1 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <May 13, 2013>

1	exp Arthroplasty, Replacement, Hip/ use mesz or Arthroplasty, Replacement/ use mesz	19032
2	exp hip arthroplasty/ use emez or exp Hip Prosthesis/	54693
3	((hip* adj2 (replacement* or arthroplast*)) or ((femoral head* or hip*) adj2 prosthes?s) or THR).mp.	111779
4	exp Arthroplasty, Replacement, Knee/ use mesz or Arthroplasty, Replacement/ use mesz	14984
5	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	32711
6	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	47964
7	or/1-6	153390
8	exp Rehabilitation/	340985
9	Rehabilitation Nursing/	1983
10	exp Rehabilitation Centers/ use mesz	11617
11	exp rehabilitation center/ use emez	8392
12	exp "Physical and Rehabilitation Medicine"/ use mesz	19217
13	exp rehabilitation medicine/ use emez	4567
14	exp rehabilitation research/ use emez	290
15	exp rehabilitation care/ use emez	7709
16	exp Physical Therapy Modalities/ use mesz	117183
17	exp physical medicine/ use emez	370105
18	exp mobilization/ use emez	15955
19	rehabilitation.fs.	156351
20	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* mobili?ation or strength train*).ti,ab.	669487
21	or/8-20	1386372
22	(Meta Analysis or Controlled Clinical Trial or Randomized Controlled Trial).pt.	472961
23	Meta-Analysis/ use mesz or exp Technology Assessment, Biomedical/ use mesz	49071
24	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	82162
25	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane or ((health technolog* or biomedical technolog*) adj2 assess*)).ti,ab.	320557
26	exp Random Allocation/ use mesz or exp Double-Blind Method/ use mesz or exp Control Groups/ use mesz or exp Placebos/ use mesz	209244
27	Randomized Controlled Trial/ use emez or exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	613192
28	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	1714134

29	exp Standard of Care/ use mesz or exp Guideline/ use mesz or exp Guidelines as Topic/ use mesz	128854
30	exp Practice Guideline/ use emez or exp Professional Standard/ use emez	545615
31	(guideline* or guidance or consensus statement* or standard or standards).ti.	227599
32	or/22-31	3111562
33	7 and 21 and 32	2422
34	limit 33 to english language	2209
35	limit 34 to yr="2008 -Current"	1202
36	remove duplicates from 35	910

CINAHL

#	Query	Results
S22	S18 AND S21	334
S21	S19 OR S20	Display
S20	((health technology N2 assess*) or meta analy* or metaanaly* or pooled analysis or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane or random* or sham*or rct* or (control* N2 clinical trial*) or guideline* or guidance or consensus statement* or standard or standards or placebo*)	Display
S19	(MH "Random Assignment") or (MH "Random Sample+") or (MH "Meta Analysis") or (MH "Systematic Review") or (MH "Double-Blind Studies") or (MH "Single-Blind Studies") or (MH "Triple-Blind Studies") or (MH "Placebos") or (MH "Control (Research)") or (MH "Practice Guidelines") or (MH "Randomized Controlled Trials")	Display
S18	S17 Limiters - Published Date from: 20080101-20131231; English Language	1,269
S17	S8 AND S16	2,333
S16	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15	294,356
S15	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* or mobilization or mobilisation or strength train*)	235,934
S14	(MH "Arthroplasty, Replacement+/RH")	1,060
S13	(MH "Arthroplasty, Replacement, Hip/RH")	490
S12	(MH "Arthroplasty, Replacement, Knee+/RH")	610
S11	(MH "Arthroplasty, Replacement"/RH)	0
S10	(MH "Rehabilitation Nursing")	2,123
S9	(MH "Rehabilitation+") OR (MH "Rehabilitation Centers+") OR (MH "Rehabilitation Patients")	166,929
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	17,339
S7	thr or tkr	906
S6	knee* N2 (replacement* or arthroplast* or prosthes*)	7,671
S5	(MH "Arthroplasty, Replacement, Knee+")	6,554
S4	(femoral head* or hip*) N2 prosthes*	353
S3	hip* N2 (replacement* or arthroplast*)	9,206
S2	(MH "Arthroplasty, Replacement, Hip")	7,932
S1	(MH "Arthroplasty, Replacement")	2,180

ALL EBM Reviews
EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 2013, EBM Reviews - ACP Journal Club 1991 to April 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2013, EBM Reviews - Cochrane Central Register of Controlled Trials March 2013, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, BM Reviews - Health Technology Assessment 2nd Quarter 2013, EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2013

#	Searches	Results
1	exp Arthroplasty, Replacement, Hip/ or Arthroplasty, Replacement/	1372
2	exp Hip Prosthesis/	932
3	((hip* adj2 (replacement* or arthroplast*)) or ((femoral head* or hip*) adj2 prosthes?s) or THR).mp.	3279
4	exp Arthroplasty, Replacement, Knee/ or Arthroplasty, Replacement/	1292
5	exp Knee Prosthesis/	473
6	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	2439
7	or/1-6	5206
8	exp Rehabilitation/ or exp Rehabilitation Nursing/ or exp Rehabilitation Centers/	11595
9	exp Physical Therapy Modalities/	11502
10	rehabilitation.fs.	427
11	(rehabilitat* or habilitat* or movement therap* or physiotherap* or physical therap* or exercis* or occupational therap* mobili?ation or strength train*).ti,ab.	37415
12	or/8-11	47922
13	7 and 12	586
14	(Meta Analysis or Controlled Clinical Trial or Randomized Controlled Trial).pt.	393714
15	Meta-Analysis/ or exp Technology Assessment, Biomedical/	458
16	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane or ((health technolog* or biomedical technolog*) adj2 assess*)).ti,ab.	33338
17	exp Random Allocation/ or exp Double-Blind Method/ or exp Control Groups/ or exp Placebos/	121735
18	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	376203
19	exp Standard of Care/ or exp Guideline/ or exp Guidelines as Topic/	1075
20	(guideline* or guidance or consensus statement* or standard or standards).ti.	6944
21	or/14-20	528911
22	13 and 21	529
23	limit 22 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	529
24	limit 23 to yr="2008 -Current" [Limit not valid in DARE; records were retained]	211
25	remove duplicates from 24	210

Appendix 2: Evidence Tables

Table A5: AMSTAR[a] Scores for Systematic Reviews

Author, Year	AMSTAR score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
Kolber et al, 2013 (7)	4	✓		✓				✓				✓

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; CADTH, Canadian Agency for Drugs and Technologies in Health.
[a] Details of AMSTAR method are described in Shea et al.(4)

Table A2: GRADE Evidence Profile for Comparison of Higher Intensity Rehabilitation and Lower Intensity Rehabilitation During the Acute Hospitalization Period After Hip Arthroplasty

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Functional Status - Iowa Level of Assistance							
1 (RCT) (6)	Serious limitations (−1)[a]	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕⊕ Moderate
Length of Stay							
1 (RCT) (6)	Serious limitations (−1)[a]	No serious limitations	Serious limitations (−1)[b]	Serious limitations (−1)[c]	Undetected	None	⊕ Very Low

Abbreviations: RCT, randomized controlled trial.
[a] See Appendix 2, Table A4 for GRADE Risk of Bias table.
[b] The study was conducted in a private hospital setting, and authors reported that patients were often expected to stay a minimum of 7 days. It was unclear how the decision to discharge patients was made. Authors stated those discharged to inpatient rehabilitation were often discharged earlier than those discharged home, and therefore hospital length of stay may not reflect improved outcomes.
[c] Study was not powered to detect a difference in hospital length of stay and does not meet the optimal information size for this outcome.

Table A3: GRADE Evidence Profile for Comparison of Higher Intensity Rehabilitation and Lower Intensity Rehabilitation During the Acute Hospitalization Period After Knee Arthroplasty

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Length of Stay							
1 (RCT) (8)	Very Serious limitations (−2)[a]	No serious limitations	No serious limitations[b]	Serious limitations[cd]	Undetected	None	⊕ Very Low

Abbreviations: RCT, randomized controlled trial
[a] See Appendix 2, Table A4 for GRADE Risk of Bias table
[b] Authors stated that discharge was scheduled for day 4 after surgery, but the flexibility for discharge was unclear
[c] All analyses were conducted at the patient level; however, there was no adjustment for clustering effect, and no account for clustering in power calculation
[d] Study was not designed or powered to detect a difference in hospital length of stay

Table A4: Risk of Bias in Randomized Controlled Trials for the Comparison of Higher Intensity Rehabilitation and Lower Intensity Rehabilitation During the Acute Hospitalization Period After Hip Arthroplasty

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Hip Arthroplasty					
Stockton & Mengersen, 2009 (6)	No limitations	Serious limitations[a]	No limitations	No limitations	No limitations
Knee Arthroplasty					
Lenssen et al, 2006 (8)	No limitations	Very serious limitations[b]	No limitations	No limitations	No limitations[c]

Abbreviation: RCT, randomized controlled trial.
[a] Morning physiotherapists were blinded to treatment allocation, however blinding was not always successful. Neither afternoon therapists nor patients were blinded. An attempt was made to blind all assessors.
[b] Neither the physiotherapist nor the patients were blinded.
[c] Cluster randomized by week of surgery rather than patient; however, it was not downgraded for sampling bias as intensity assignment was not given until the day of the surgery and patient groups appeared to be balanced at baseline although no statistical analysis provided. The intracluster correlation efficient was small.

Reference List

(1) Bone and Joint Canada. Hip and knee replacement surgery toolkit. Canada: Bone and Joint Canada; 2009. 79 p.

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(3) British Orthopaedic Association. Primary total hip replacement: a guide to good practice. London: British Orthopaedic Association; 2012 [cited 2013 Jul 5]. 38 p. Available from: http://www.britishhipsociety.com/uploaded/Blue%20Book%202012%20fsh%20nov%202012.pdf

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(5) Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr; 64(4):380-2.

(6) Stockton KA, Mengersen KA. Effect of multiple physiotherapy sessions on functional outcomes in the initial postoperative period after primary total hip replacement: a randomized controlled trial. Arch Phys Med Rehab. 2009;90(10):1652-7.

(7) Kolber MJ, Hanney WJ, Lamb BM, Trukman B. Does physical therapy visit frequency influence acute care length of stay following knee arthroplasty? A systematic review. Top Geriatr Rehabil. 2013;29(1):25-9.

(8) Lenssen A, Crijns Y, Waltje E, van Steyn M, Geesink R, van den Brant PA et al. Efficiency of immediate postoperative inpatient physical therapy following totalknee arthroplasty: an RCT. BMC Musculoskelet Disord. 2006;7:71: DOI: 10.1186/1471-2474-7-71.

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