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CADTH OPTIMAL USE REPORT

Optimal Use of Minimally Invasive Glaucoma Surgery: Recommendations

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Abbreviations

AE	adverse event
ELSI	ethical, legal, and social issues
HTA	Health Technology Assessment
HTERP	Health Technology Expert Review Panel
ICUR	incremental cost-utility ratio
IOP	intraocular pressure
MIGS	minimally invasive glaucoma surgery
QALY	quality-adjusted life-year
QoL	quality of life

Summary of Recommendation

These recommendations were developed by the Health Technology Expert Review Panel (HTERP) based on evidence reviewed in a CADTH Health Technology Assessment (HTA) report.[1] The HTA included a review of the clinical effectiveness and safety, cost-effectiveness, patients' and caregivers' perspectives and experiences, ethical issues, and implementation issues regarding minimally invasive glaucoma surgery (MIGS) for the treatment of adults with glaucoma.

The information retrieved and the HTERP deliberations aimed to address the policy questions: What is the optimal use, including appropriate patient selection, of MIGS devices and procedures for adults with glaucoma? Should MIGS devices and procedures be funded by the public health care system?

The target population for these recommendations is patients with glaucoma who are deemed eligible for MIGS by their care provider. The target users of these recommendations are Canadian health care decision-makers, those in provincial and territorial ministries of health, and glaucoma researchers.

1. HTERP considered that there is insufficient evidence at present to make recommendations specific to the optimal use and funding of MIGS.
2. HTERP suggests that there is a potential role for MIGS devices and procedures in the treatment of adult patients with glaucoma, if the choice of MIGS is presented to patients with full consideration and disclosure of relevant factors, including:
   - the diversity of MIGS options, and uncertainties and unknowns associated with their benefits and risks
   - individual patient factors bearing on the choice of treatment (e.g., vulnerabilities, geographical location, and financial considerations)
   - the surgeon's experience performing MIGS and potential conflicts of interest
   - alternative forms of treatment.
3. HTERP suggests that provinces and territories establish harmonized procedure codes for MIGS (to enable surveillance of access and treatment patterns) and document actual costs associated with MIGS and alternative treatments.
4. HTERP suggests that the optimal use, including funding, of individual MIGS be reassessed if further research is conducted that includes: detailed reporting of results stratified by patient characteristics; valid and reliable measures of direct, patient-important outcomes; and long-term evaluation of clinical effectiveness, adverse events, harms, and cost-effectiveness.

Technology

MIGS are devices and procedures that are used with the aim of lowering the pressure inside the eye (intraocular pressure; [IOP]) by improving outflow of eye fluid, or reducing its inflow, while being less invasive than traditional surgery (i.e., no dissection of the sclera and minimal or no manipulation of the conjunctiva).[2-4] As of June 2018, there were 11 MIGS devices and procedures approved for use in Canada; one device (CyPass Micro-Stent) was subsequently voluntarily withdrawn from the global market by the manufacturer in August 2018 based on data from a long-term five-year safety study (unpublished data).[5] Although MIGS are collectively categorized as a class of interventions, each MIGS is unique in its structure and/or mechanism of action. The MIGS options may be grouped according to the approach for reducing IOP:

- Reducing the production of eye fluid (i.e., endoscopic cyclophotocoagulation)
- Increasing the outflow of eye fluid through the trabecular meshwork using:
  - tissue ablation or removal (i.e., Trabectome and Kahook Dual Blade)
  - a device (i.e., iStent, iStent Inject, or Hydrus Microstent)
  - 360º suture (i.e., gonioscopy-assisted transluminal trabeculotomy [GATT])
- Increasing outflow through the uveoscleral route via suprachoroidal shunts (i.e., CyPass Micro-Stent)
- Increasing outflow through a subconjunctival pathway (i.e., XEN 45 Gel Stent, XEN 63 Gel Stent, and XEN 140 Gel Stent).

MIGS can be performed alone or in combination with cataract surgery, which also independently lowers IOP.

Methods

CADTH conducted an HTA on the clinical effectiveness and safety, cost-effectiveness, patients' and caregivers' perspectives and experiences, ethical issues, and implementation issues of MIGS for the treatment of adults with glaucoma.[1] HTERP developed recommendations on the appropriate use of MIGS based on the evidence presented in the HTA report. HTERP members reviewed the evidence, discussed all elements of the HTERP deliberative framework,[6] considered stakeholder feedback, and developed recommendations through discussion, deliberation and voting. Additional information on the HTERP process is found on the HTERP page of the CADTH website.

Detailed Recommendation

The objective of these recommendations is to provide advice for Canadian health care decision-makers, those in provincial and territorial ministries of health, and glaucoma researchers, about the use and study of MIGS.

1. HTERP considered that there is insufficient evidence at present to make recommendations specific to the optimal use and funding of MIGS.
2. HTERP suggests that there is a potential role for MIGS devices and procedures in the treatment of adult patients with glaucoma, if the choice of MIGS is presented to patients with full consideration and disclosure of relevant factors, including:
   - the diversity of MIGS options, and uncertainties and unknowns associated with their benefits and risks
   - individual patient factors bearing on the choice of treatment (e.g., vulnerabilities, geographical location, and financial considerations)
   - the surgeon's experience performing MIGS and potential conflicts of interest
   - alternative forms of treatment.
3. HTERP suggests that provinces and territories establish harmonized procedure codes for MIGS (to enable surveillance of access and treatment patterns) and document actual costs associated with MIGS and alternative treatments.
4. HTERP suggests that the optimal use, including funding, of individual MIGS be reassessed if further research is conducted that includes: detailed reporting of results stratified by patient characteristics; valid and reliable measures of direct, patient-important outcomes; and long-term evaluation of clinical effectiveness, adverse events, harms, and cost-effectiveness.

Rationale

- There was insufficient evidence for the comparative clinical effectiveness and safety of MIGS (with or without cataract surgery) versus each other and versus alternative current glaucoma treatments. However, the available evidence for the effectiveness of MIGS was largely neutral (i.e., MIGS were neither more nor less effective than alternative treatments) and most adverse events (AEs) were considered minor.
- Although MIGS are a "class" of interventions, each MIGS is unique in its structure and/or mechanism of action, and different MIGS may have different clinical effectiveness or safety profiles. There was no definitive evidence regarding which MIGS might be preferable, either overall or for a subset of patients; additional studies with head-to-head comparisons of different MIGS are required.
- Economic analyses from the Canadian health care payer's perspective found that the incremental differences in quality-adjusted life-years (QALYs) were relatively small over a lifetime time horizon and were subject to a very high level of uncertainty. Similarly, incremental differences in cost were small between strategies and the models were found to be sensitive to the total cost of MIGS.
- Several assumptions were required to construct the economic models, and future work may confirm or refute these assumptions. The results suggested that, if used indiscriminately, MIGS may not always be the cost-effective option in certain patients.

- Provincial systems and health facilities have different policies on billing (e.g., public coverage, out-of-pocket payment, and third-party insurance), and fees vary across Canada. The absence of fee codes in most provincial schedules of benefits for MIGS in most jurisdictions means that proxy codes are frequently used, which can result in disproportionate physician reimbursement. Additionally, the absence of procedure codes makes estimation of the true prevalence of use and the costs associated with MIGS difficult.
- MIGS are currently delivered on the basis of surgeon- or site-specific factors and there is wide variation in access to MIGS (both generally and with respect to specific devices and procedures). There is support for MIGS from professional ophthalmological associations, but no formal credentialing and no evidence-based guidance on patient selection and the place for MIGS in the care trajectory; MIGS are offered at the discretion of the health care provider. Barriers to implementation include funding challenges (e.g., high start-up costs and finite budgets for facilities), and the need for strong ophthalmology leadership and operating rooms.
- Some patients value freedom from eye drops; however, the extent to which MIGS reduces the need for pharmacotherapy in comparison with other currently available treatments is unclear. There was variability in patients' willingness to accept the risks of surgery (including MIGS). Some patients preferred to follow the recommendation of their trusted health care provider, while others desired shared decision-making; patient-provider relationships were reported as a central component of patients' experiences of glaucoma and its treatment. Individual factors influenced perceptions of acceptability of MIGS (e.g., vulnerabilities such as old age, geographical location, and capacity to pay non-insured or out-of-pocket costs associated with choosing MIGS compared with other treatment options).
- Manufacturers provide research funding and surgeon training to support adoption of MIGS devices and procedures. There is a need to disclose and manage potential conflicts of interest.
- Additional information is needed to inform the optimal use, including funding, of MIGS. Specifically, there is a need for detailed reporting and stratification of results by patient characteristics (e.g., type and severity of glaucoma); valid and reliable measures of direct, patient-important outcomes (e.g., health-related quality of life); and systematic long-term evaluation of clinical effectiveness, AEs, harms, and cost-effectiveness.

Considerations

As HTERP worked the MIGS topic through its deliberative framework, the following considerations were put forth as part of their discussion.

HTERP considered the clinical evidence,[1] which indicated that the comparative clinical effectiveness and safety of MIGS versus each other and versus alternative glaucoma treatments currently in practice was largely unclear. Specifically, there was insufficient evidence for the comparative clinical effectiveness and safety for MIGS versus pharmacotherapy, laser therapy, different MIGS (i.e., one type of MIGS versus another) or filtration surgery, and there was insufficient evidence for MIGS in combination with cataract surgery versus a different MIGS in combination with cataract surgery or filtration surgery in combination with cataract surgery. The clinical effectiveness of MIGS in combination with cataract surgery tended to be more favourable than cataract surgery alone; however,

findings for comparative safety were mixed. Most reported AEs were considered minor in all treatment groups; however, when major AEs were observed, between-group differences were uncertain. There was insufficient evidence directly comparing the clinical effectiveness or safety of different MIGS, and there was no definitive evidence regarding which MIGS might be preferable, either overall or for a subset of patients. HTERP acknowledged that, although the data were limited, the available evidence was largely neutral (i.e., insufficient evidence for MIGS being either more or less effective than alternative treatments).

HTERP acknowledged that the clinical findings were based largely on "very low" or "low" quality evidence (according to the Grading of Recommendations Assessment, Development and Evaluation [GRADE] framework) for surrogate or indirect end points (i.e., IOP and number of medications as surrogates for visual field and quality of life respectively). Only one study reported on the primary outcome of quality of life (QoL). Additional information on health-related QoL and patient-reported outcomes, with long-term follow-up, is needed.

Furthermore, HTERP recognized that the clinical evidence should be interpreted with caution, given that, although MIGS are categorized as a particular class of interventions each is unique in terms of its structure and mechanism of action, and may reasonably be anticipated to have different clinical effectiveness and safety profiles. For example, one device (CyPass Micro-Stent) was voluntarily withdrawn from the market by the manufacturer due to safety concerns in August of 2018.[5] Although these safety concerns are unlikely to extend to other MIGS devices and procedures,[7] this highlights the challenges in developing recommendations for a class of heterogeneous treatments. Differences in the use of these devices and procedures can also include differences in the learning curves for surgeons and differences in the amount of time required in the operating room.

HTERP also acknowledged that the inconclusive findings of the Clinical Review tended to be at odds with the perspectives of some practising ophthalmologists who provided feedback on the HTA[8] and who expressed belief in the effectiveness of MIGS for their patients. Indeed, there is broad agreement among glaucoma specialists that MIGS have a role in the glaucoma treatment algorithm.[9] Stakeholder feedback received in the form of a letter signed by most members of the Canadian Glaucoma Society endorsed the use of MIGS. HTERP's deliberations on these recommendations were based on the current available evidence (summarized below and documented in the CADTH *Optimal Use of Minimally Invasive Glaucoma Surgery: A Health Technology Assessment* report[1]). This disparity between the existing evidence and the quality of the evidence on the clinical effectiveness of MIGS, and the adoption of MIGS by Canadian specialists and hospitals to date was further considered in the Ethical Issues Analysis of the report. In particular, in the context of surgical innovation, adequate oversight and informed consent, including full candour about the clinical unknowns and uncertainties around MIGS, are complicated responsibilities.

HTERP considered the evidence from the economic evaluation in the HTA,[1] which revealed that MIGS may economically be more attractive than pharmacotherapy for eligible patients from the Canadian health care payer's perspective. MIGS were more costly and less effective than laser therapy in patients with mild glaucoma. If performed alongside cataract surgery, the incremental cost-utility ratio (ICUR) for MIGS was $63,626 per QALY compared with cataract surgery alone; however, the ICUR range across different MIGS devices was $11,963 per QALY to $137,947 per QALY, suggesting that some MIGS were cost-effective while others were not, depending on one's willingness-to-pay. In comparisons with filtration surgery (i.e., MIGS versus filtration surgery, or MIGS plus cataract surgery versus filtration

surgery plus cataract surgery), MIGS were less costly but also less effective. All of the economic results were subject to a high level of uncertainty, as evidenced by the results of the sensitivity and probabilistic analyses. Overall, the findings suggested that, if used indiscriminately, MIGS may not always be the cost-effective treatment option in certain patients.

HTERP recognized that the underlying clinical evidence incorporated into the economic evidence was generally of poor quality, as noted above. Furthermore, several assumptions were required to construct the economic models, including extrapolating short-term evidence into a lifetime time horizon. Sensitivity analyses indicated that the economic findings were also sensitive to changes in comparative treatment effects and total costs of MIGS, both of which had substantial uncertainty (e.g., based on the current clinical evidence and jurisdictional variability in costs). In addition, the absence of fee codes for MIGS surgery in most jurisdictions (i.e., in all provinces except Alberta and Quebec) means that providers of MIGS must use proxy fee codes that approximate the time, complexity, or cost of performing MIGS. If there is no suitable proxy billing code, physicians could bill for procedures that are not reflective of the costs or length of MIGS procedures. The lack of procedure codes makes estimating true prevalence of use and costs associated with MIGS difficult.[10] Sensitivity analyses employing different physician billing approaches were therefore conducted in scenario analyses from the Ontario perspective.

As the economic evaluation was conducted from the perspective of the Canadian health care payer, direct and indirect costs to patients were not considered. However, the Patients' and Caregivers' Perspectives and Experiences Review team engaged with patients who described the systemic burdens of having to travel to access MIGS and follow-ups that included direct (e.g., cost of gas, hotel stays, and meals) and indirect (e.g., time off work) personal costs.

In addition to cost considerations that may impact access to MIGS, HTERP considered additional patient- and system-level equity of access issues that were identified. Specifically, there is ad hoc distribution of opportunities for MIGS and availability of specific devices, with no evidence of equitable outcomes in distribution. Provincial systems and health facilities have different policies on billing (public coverage, out-of-pocket payment, and third-party insurance), and fees vary across Canada. Diverging views of MIGS as an "optional upgrade" or a "medical need" create policy inconsistencies and may put vulnerable patients in situations of difficult choice, sometimes to the detriment of health outcomes. Patients living in rural and remote locations have less access to specialists, are sometimes referred to specialists too late for MIGS to be a viable option, and incur out-of-pocket travel expenses for surgery and follow-ups. Known inequities exist in the incidence and severity of glaucoma among racialized groups outside Canada (based on socioeconomic and potential genetic factors), but little is known about Canadian populations per se.

HTERP acknowledged that the ethics of surgical innovation should also be considered. In the context of surgical innovation, specialists and health institutions may be vulnerable to conflicts of interest, industry influence, and innovation bias, and this seems to be true of MIGS use in Canada. At present, manufacturers provide the majority of training, which helps support the adoption of their devices. It is unclear who is responsible for ongoing tracking, analyzing and reporting on outcomes of specific MIGS devices in order to inform optimal use. Supporting patients' choices requires that specialists fully disclose the current

innovation context of MIGS options and outcomes compared with traditional treatment options.

HTERP considered the perspectives and experiences of patients with glaucoma. Pharmacotherapy in the form of eye drops is disruptive to patients' lives (e.g., impracticality, difficulty with administration, side effects), and reducing the number and frequency of medications is of value to some patients. However, whether MIGS were more efficacious in reducing the number of medications in comparison with other treatment options (e.g., laser therapy or filtration surgery) was unclear. There was greater variability in patient preferences with respect to more invasive surgeries, with some patients equating surgery to freedom from eye drops and others being more conservative regarding the risks of surgery (including blindness) and viewing surgery as a last resort. Patients who had undergone MIGS expressed similarly varied perceptions in regard to the balance of benefits and risks, and noted patient-provider relationships made a difference in patients' views of the acceptability of surgeries (including MIGS). Some patients expressed willingness to proceed with surgery based on the advice of their treating physician; others expressed interest in shared decision-making.

HTERP also recognized that patient-provider relationships are central to patients' experiences with glaucoma treatment and provide an opportunity to assist patients to become more knowledgeable about glaucoma, improve adherence, and adjust to vision changes. Having strong ophthalmology leadership and operating rooms that favour new technologies such as MIGS can be an enabler to their use and an enabler for acquiring adequate funding. However, there are no credentialing standards for MIGS. Although professional societies (including the Canadian Glaucoma Society and Canadian Ophthalmological Society) endorse the use of MIGS, there are a lack of evidence-based clinical practice guidelines detailing appropriate patient selection for and use of MIGS devices and procedures.

HTERP noted that future research is needed to fill the evidence gaps that are particularly relevant to the Canadian context, given the geographical spread of the Canadian population and the need to provide care in diverse settings (e.g., rural and remote areas) to people with diverse needs (e.g., racialized groups based on socioeconomic and potential genetic factors). From a clinical perspective, long-term follow-up from head-to-head study designs is needed to inform the comparative clinical effectiveness and safety of MIGS over time. Detailed reporting and stratification of results by patient characteristics (e.g., type and severity of glaucoma) will assist with appropriate patient selection. Particularly in the context of inconclusive clinical outcomes, increased attention to patient-important outcomes such as health-related QoL (assessed using valid and reliable measures), is imperative. From an economic perspective, there is variability in costs within and across jurisdictions, and detailed micro-costing of MIGS and comparator interventions may allow for greater certainty in the true absolute and incremental costs of MIGS to better inform their potential economic value. Establishment of harmonized provincial and territorial procedure codes for MIGS will enable surveillance of use and actual costs. Qualitative studies concerning MIGS specifically are needed to inform patients' experiences with glaucoma surgeries including MIGS, providers' experiences and perceptions of caring for patients with glaucoma, and perspectives of specialists who have decided in favour of or against using MIGS in treating glaucoma patients. Ethical and social concerns that require further exploration include knowledge of how glaucoma treatment in general and MIGS treatment options in particular intersect with racialized groups within Canada, and whether and how specialists can

reasonably incorporate patients' circumstantial details (e.g., financial means, geographical constraints) into informed-consent discussions around potential choice of treatment. Implementation analyses would benefit from consideration of additional factors, including setting, epidemiology, socioeconomic, sociocultural, political, and legal aspects.

Given the many areas of uncertainty, HTERP considered that there is insufficient evidence at present to make recommendations specific to the optimal use and funding of MIGS. HTERP also considered that reassessment of the optimal use of MIGS, including funding, would be of value if sufficient future research is conducted that addresses these areas of uncertainty. However, HTERP recognized that there is a potential role for MIGS devices and procedures in the treatment of adult patients with glaucoma under certain conditions.

Evidence

The complete clinical, economic, patient's and caregivers' preferences and experiences, ethical issues, and implementation evidence used for developing this guidance is available in the CADTH *Optimal Use of Minimally Invasive Glaucoma Surgery: A Health Technology Assessment* report.[1]

Clinical Evidence

The clinical evidence was addressed in a systematic review of primary studies. The questions were:

- What is the comparative clinical effectiveness of MIGS devices and procedures versus each other, pharmacotherapy, laser therapy, or filtration surgery, for the treatment of glaucoma in adults?
- What is the comparative safety of MIGS devices and procedures versus each other, pharmacotherapy, laser therapy, or filtration surgery, for the treatment of glaucoma in adults?
- What is the comparative clinical effectiveness of MIGS devices and procedures performed in combination with cataract surgery versus a different MIGS plus cataract surgery, filtration surgery plus cataract surgery, or cataract surgery alone for the treatment of glaucoma in adults?
- What is the comparative safety of MIGS devices and procedures performed in combination with cataract surgery versus a different MIGS plus cataract surgery, filtration surgery plus cataract surgery, or cataract surgery alone for the treatment of glaucoma in adults?

There were 32 included studies (35 publications; 10 randomized controlled trials, two non-randomized controlled trials, and 20 observational studies). Across the studies, the mean patient age ranged from 54 to 79 years, men and women were equally represented, the majority of patients were White, and patients with mild-to-moderate open-angle glaucoma were most commonly included. Overall, there was insufficient evidence to determine the comparative clinical effectiveness and safety of MIGS versus pharmacotherapy, laser therapy, different MIGS (i.e., one type of MIGS versus another), or filtration surgery. The clinical effectiveness of MIGS in combination with cataract surgery tended to be more favourable than cataract surgery alone, however findings for comparative safety were mixed. There was insufficient evidence for the comparative clinical effectiveness and safety of

MIGS in combination with cataract surgery versus a different MIGS in combination with cataract surgery or versus filtration surgery in combination with cataract surgery. However, these conclusions were based largely on “very low” or “low” quality evidence (e.g., due to concerns with risk of bias) for indirect end points (i.e., IOP and number of medications as surrogates for visual field and QoL, respectively). Only one study included a QoL outcome, and the measure did not consider the number of glaucoma medications that would be expected to impact QoL. The majority of AEs were considered minor in all treatment groups; however, between-group differences were uncertain when major AEs were reported. The evidence for AEs was “very low” quality, in part because the method of measuring AEs was not reported in any study (therefore, it is uncertain whether there was any restriction on what was considered an AE, whether data on all patient-important AEs were collected, or whether information was captured systematically across patients or by convenience [e.g., in only those patients who returned to the study centre for treatment]).

In addition, this evidence should be interpreted with caution, given that, although MIGS are categorized as a particular class of interventions each is unique in terms of its structure and mechanism of action, and may reasonably be anticipated to have different clinical effectiveness and safety profiles. There was insufficient evidence to offer specific conclusions regarding individual MIGS devices and procedures, and there was no definitive evidence regarding which MIGS might be preferable, either overall or for a subset of patients.

Economic Evidence

The economic evaluation was comprised of a Markov cohort model, which was constructed to examine the cost-effectiveness of MIGS, with or without cataract surgery, compared with alternative treatments during a patient’s lifetime from a Canadian health care payer perspective. The question addressed was:

- What is the cost-effectiveness of MIGS devices and procedures versus each other, pharmacotherapy, laser therapy, or filtration surgery, for the treatment of glaucoma in adults?

The clinical pathway and decision-analytic model were developed by reviewing existing clinical and economic literature, and the conceptualization of the model and its structure was subsequently validated by clinicians with expertise in ophthalmology. Health states in the model were defined based on disease severity according to the Hodapp-Parrish-Anderson score with death as an absorbing health state. The effects of treatment in terms of change in IOP were taken from the Clinical Review and were incorporated into the rate of glaucoma progression as defined by visual field. In patients entering the model at a mild or moderate severity stage, trabeculectomy was assumed to be offered to patients upon transitioning to an advanced stage of glaucoma. The primary outcome was cost per QALYs gained, in 2018 Canadian dollars and all base-case analyses were probabilistic. The base case was based on Alberta costing, and separate scenario analyses were conducted using an Ontario setting.

It was not possible to examine scenarios where multiple treatment options might be suitable for patients. The reference case findings suggested that there were some comparisons where MIGS may be cost-effective whereas, in other cases, MIGS were unlikely to be economically attractive. Specifically, in patients with moderate glaucoma, the ICUR for MIGS compared with pharmacotherapy was found to be $18,808 per QALY; whereas, MIGS was

found to be dominated by laser surgery in patients with mild glaucoma (i.e., MIGS was more costly and less effective). If performed alongside cataract surgery, the ICUR for MIGS was $63,626 per QALY (range across different MIGS devices: $5,984 per QALY to $108,934 per QALY) compared with cataract surgery alone. In comparisons with filtration surgery (i.e., MIGS versus filtration surgery, or MIGS plus cataract surgery versus filtration surgery plus cataract surgery), MIGS were less costly but also less effective. Among all models, the incremental difference in QALYs and costs were relatively small and the findings were sensitive to changes in comparative treatment effects and initial surgery-related costs. Expected differences in QALYs between comparisons were accumulated over a long time period in the economic model; yet, there was limited clinical evidence beyond one year follow-up. Variability in costs exists between settings and jurisdictions, and uncertainty remains regarding the true costs of MIGS in some jurisdictions where they are not currently performed or publicly funded. All results were subject to a very high level of uncertainty as shown by the probabilistic analyses. For instance, at a willingness-to-pay threshold of $100,000 per QALY, MIGS had a probability of being cost-effective approximately 65% of the time. Caution is required in interpreting these findings given the uncertainty in relative efficacy and costs and the lack of long-term data.

Patients' and Caregivers' Perspectives and Experiences Evidence

The patients' and caregivers' perspectives and experiences evidence was addressed in a systematic review and thematic synthesis of primary qualitative research describing the perspectives and experiences of patients with glaucoma and of their caregivers. Patients were engaged throughout the project, in the form of conversations with three female patients with glaucoma, two of whom had undergone MIGS. The question addressed was:

- What are the perspectives and experiences of patients with glaucoma regarding glaucoma and their treatment, and of their caregivers?

The results of the thematic synthesis centered around patients' experiences and perceptions of glaucoma. First, a diagnosis of glaucoma is unexpected. Typically patients explain vision changes as part of normal aging, not as a prompt to seek vision care. This means that those without routine vison care may be more at risk for being diagnosed with more advanced glaucoma and therefore be ineligible for MIGS. Second, glaucoma is invisible in that glaucoma is something most patients are not initially aware of and that is not experienced directly; rather, glaucoma is largely asymptomatic until vision changes are substantial. In addition, glaucoma is invisible to others — others cannot see vision loss. Third, patients equated glaucoma as blindness and feared becoming blind, and wished to preserve their remaining sight. Fourth, pharmacotherapy in the form of eye drops is disruptive to patients' lives. Despite a range of creative and committed responses, adherence is difficult among patients with comorbidities and busy lives (e.g., with travel or lack of routine). Reducing the number and frequency of medications is of value to some patients. Fifth, patients expressed a range of views on glaucoma surgeries, from surgeries being a last resort to surgeries meaning freedom from eye drops. Some patients may be more conservative in assuming the risks of surgery, including possible blindness. Lastly, patients experience glaucoma as an illness, not as a disease. This means that a patient's experience of glaucoma is shaped by, but not reducible to, their clinical condition. While surgical treatments can offer patients improved clinical outcomes, patients may still worry about the need to take additional

medications or to have future surgery and the need for vigilance about the return of elevated IOP, pointing to the lingering impact of glaucoma.

Ethics Evidence

The ethics evidence was addressed in a literature search using a peer-reviewed search strategy, with methodological filters applied to limit retrieval to studies related to ethical, legal, and social issues (ELSI). The search was limited to English- or French-language publications. No relevant studies were identified. For this reason, the selection criteria were broadened to include bodies of research and commentary that dealt with issues indirectly or analogously related to potential ethical issues identified through expert recommendations and through a CADTH Environmental Scan titled *"Minimally Invasive Glaucoma Surgery: Implementation Considerations."*[11] The questions addressed were:

- What are the major ethical issues raised by the use of MIGS devices and procedures?
- What are the broader legal, social, and cultural considerations?

Results identified two major facts around the current usage of MIGS that bear on the analysis of ethical and social aspects of the optimal use of MIGS in Canada. First, there is a disparity between the existing quality of evidence on the clinical effectiveness of MIGS and the belief in its value manifested in the adoption of MIGS by Canadian specialists and hospitals to date. Second, current usage of MIGS in Canada is not strongly evidence-based, standardized, or personalized to the needs of patients. For example, MIGS are unevenly available across Canada; MIGS tend to be used according to surgeon preference, training, experience, and comfort level; and the allocation of MIGS devices to patients currently proceeds without objective criteria, subject to surgeon discretion.

In addition, results from the literature review and other sections of this HTA identified two main categories of issues that capture ethical and social concerns relevant to considering the optimal use of MIGS in Canada: equity of access and the ethics of surgical innovation. Ethical concerns related to equity of access include: whether and under what conditions there can be equitable access for Canadians treated in different health care systems and facilities, for those living in rural and remote versus more urban locations, and for those belonging to various racial or ethnic groups. Requiring private payment for MIGS as a premium device raises equity questions for patients with different economic capacities to incur out-of-pocket costs associated with such a model of implementation. Concerns with the status of MIGS as a surgical innovation require ensuring that conflicts of interest in the use of MIGS are disclosed and managed, and that evidence on outcomes is gathered and assessed. They also demand that professionals carry out their responsibility to ensure that patients are fully informed about options, evidence, and other relevant issues surrounding their potential choice of MIGS.

Implementation Evidence

The implementation evidence was informed by the CADTH Environmental Scan titled *"Minimally Invasive Glaucoma Surgery: Implementation Considerations"* that comprised a narrative literature review and consultations with targeted key informants.[11] The question addressed was:

- What are the challenges and enablers affecting the use of MIGS devices and procedures in Canada for the treatment of adult patients with glaucoma?

In total, 21 key informants were interviewed and data from 21 relevant publications were used to inform the analysis. Several important barriers and facilitators to the implementation of MIGS in Canada were identified.

First, the majority of provinces and territories (except Quebec and Alberta) do not have MIGS devices or procedures in the physician schedule of benefits, and they are not a publicly insured benefit. MIGS are often provided at a cost to the facility or at a cost to the patient, which can pose an ethical issue regarding health care and ability to pay. Funding challenges, high start-up costs, and finite budgets for facilities with the ability to provide MIGS devices can be prohibitive to their implementation.

In terms of setting, patients who live closer to a facility providing MIGS are more likely to be able to receive the surgery. However, not all MIGS devices and procedures are available at every facility; therefore, proximity to a glaucoma centre is not necessarily a facilitator in all cases.

Having strong ophthalmology leadership and operating rooms that favour new technologies such as MIGS can be an enabler to their use and an enabler for acquiring adequate funding. In comparison to smaller regions or facilities, larger or more urban regions may be more able to attract glaucoma specialists who have the ability to perform MIGS. However, the relative lack of trained ophthalmologists and the lack of appropriate credentialing or standards create barriers for implementation of MIGS devices and procedures. Currently, manufacturers provide much of the training for MIGS. Despite this, and support from glaucoma professional societies (including the Canadian Glaucoma Society and Canadian Ophthalmological Society in the form of a 2017 Position Statement[9] indicating MIGS for use in patients with mild-to-moderate glaucoma), there are a lack of clinical practice guidelines detailing appropriate patient selection and use of MIGS devices and procedures. This can contribute to the uncertainty of the placement of MIGS in the glaucoma treatment paradigm.

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Appendix 1: HTERP

The Health Technology Expert Review Panel (HTERP) consists of up to seven core members appointed to serve for all topics under consideration during their term of office, and up to five expert members appointed to provide their expertise for a specific topic. For this project, three expert members with expertise in ophthalmology were appointed. The core members include health care practitioners and other individuals with expertise and experience in evidence-based medicine, critical appraisal, health technology assessment, bioethics, and health economics. One public member is also appointed to the core panel to represent the broad public interest.

HTERP is an advisory body to CADTH and is convened to develop guidance or recommendations on non-drug health technologies to inform a range of stakeholders within the Canadian health care system. Further information regarding HTERP is available at https://cadth.ca/collaboration-and-outreach/advisory-bodies/health-technology-expert-review-panel.

HTERP Core Members

Dr. Hilary Jaeger (Chair)

Dr. Jenny Basran

Dr. Jeremy Petch

Dr. Lynette Reid

Ms. Tonya Somerton

Dr. Jean-Eric Tarride

Expert Members

Dr. Neeru Gupta

Conflict of Interest

HTERP core members' declarations are posted on the CADTH website.

Dr. Neeru Gupta has received funding as a consultant to Senju Pharmaceuticals, Valeant, Allergan, and Bausch and Lomb, and as a speaker for Alcon.