ONTARIO HEALTH TECHNOLOGY ASSESSMENT SERIES

Paclitaxel-Coated Balloon Dilation for Adults With Recurrent Bulbar Urethral Stricture

A Health Technology Assessment

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Ontario Health

Key Messages

What Is This Health Technology Assessment About?

The male urethra is a tube-like structure that allows urine to pass from the bladder during urination. Bulbar urethral stricture is a condition in which there is a narrowing of a portion of the urethra, creating difficulty urinating, including incomplete bladder emptying. It can contribute to urinary tract infections.

Patients are usually treated first through either the insertion of a tool into the urethra that uses pressure to expand the narrow part or by making a cut through the stricture to widen the lumen. Stricture recurrence (relapse, or return of the condition) is common after these procedures due to scarring. The most durable but invasive and complex treatment is to release the stricture with open surgery. A new alternative to open surgery is the paclitaxel-coated balloon that uses a balloon coated with a drug called paclitaxel to widen the urethra. The paclitaxel coating is thought to help minimize scar tissue formation and postpone stricture recurrence.

This health technology assessment looked at how safe, effective, and cost-effective paclitaxel-coated balloon dilation is for adults with recurrent bulbar urethral stricture. It also looked at the budget impact of publicly funding paclitaxel-coated balloon dilation and at the experiences, preferences, and values of people with bulbar urethral stricture.

What Did This Health Technology Assessment Find?

There are no studies comparing paclitaxel-coated balloon dilation with the use of a laser or a surgical knife to make a cut in the scar tissue, which is the most common treatment method for bulbar urethral stricture in Ontario. Evidence from 1 trial found that people undergoing paclitaxel-treated balloon dilation were less likely to need another procedure within 1 year. However, this result may be overestimated because some participants were removed from the analysis in a way that favoured the intervention group. There is some evidence that this treatment improves urinary symptoms and urine flow rate better than other minimally invasive treatment methods. There are some short-term negative effects such as blood in the urine and painful urination, but these effects subside after about a month.

Compared with usual care, paclitaxel-coated balloon dilation could be less costly and more effective. We estimate that publicly funding paclitaxel-coated balloon dilation in adult males with recurrent bulbar strictures is potentially cost saving, with net savings of about $0.74 million for treating 2,747 adult males in Ontario over the next 5 years. Our economic analysis results should be interpreted with caution because of limitations in the currently published clinical evidence.

People we spoke with viewed paclitaxel-coated balloon dilation favourably because it is a minimally invasive procedure. Barriers to access include lack of awareness of the procedure, the out-of-pocket cost, and geography (because the procedure is available in only a limited number of publicly funded hospitals and private clinics).

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Citation

TBA

A Note About Terminology

As a government agency, Ontario Health can play an active role in ensuring that people of all identities and expressions recognize themselves in what they read and hear from us. We recognize that gender identities are individual and therefore in this health technology assessment we use gender-inclusive pronouns and terms as much as possible. The results of this health technology assessment apply to the male sex as well as to individuals who may not identify themselves as male but have the anatomical features of the male sex urinary system. When citing published literature that uses the terms "man" or "male," we also use these terms for consistency with these cited studies.

In this health technology assessment, we use the phrases:

- "Paclitaxel-coated balloon catheter" to describe the device
- "Paclitaxel-coated balloon dilation" to describe dilation with the paclitaxel-coated balloon catheter
- "The paclitaxel-coated balloon dilation procedure" to describe the dilation procedure performed with a paclitaxel-coated balloon catheter

Endoscopic treatment versus endoscopic management: These overlapping terms refer generally to the non-surgical technique of using an endoscope to deliver treatment to a specific region of the body without the need for an incision. An **endoscopic treatment** is a procedure to relieve a symptom or condition. **Endoscopic management** is a broader term describing the management of a condition through the use of endoscopic treatments.

Abstract

Background

Bulbar urethral stricture is the narrowing of the bulbar segment of the urethra, which causes urinary symptoms and difficulty in voiding. Surgical urethroplasty is the gold standard treatment, but usually the first-line treatment is using either a simple (uncoated) balloon, a rigid dilator, or performing direct vision internal urethrotomy, which uses a blade or laser to make a cut in the stricture. Treatment with a balloon that is coated with paclitaxel has been offered as a second-line treatment when the stricture recurs. This health technology assessment looked at how safe, effective, and cost-effective paclitaxel-coated balloon dilation is for adults with recurrent bulbar urethral stricture. It also looked at the budget impact of publicly funding paclitaxel-coated balloon dilation and at the experiences, preferences, and values of people with bulbar urethral stricture.

Methods

We performed a systematic literature search and reviewed the clinical evidence and the economic evidence. We assessed the risk of bias in the study using RoB 2 and JBI tools and the quality of the body of clinical evidence according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. We developed a probabilistic state-transition (Markov) model to conduct a cost-effectiveness analysis over the 5-year horizon from a public payer perspective. We compared urethral dilation with the paclitaxel-coated balloon catheter to usual care (i.e., endoscopic management represented by a mix of urethral dilation procedures and direct vision internal urethrotomy) for adult males with recurrent bulbar urethral strictures. We also analyzed the 5-year budget impact of publicly funding this technology in eligible adult males in Ontario. To contextualize the potential value of paclitaxel-coated balloon dilation, we aimed to speak with adults and care partners in Ontario who had lived experience with bulbar urethral strictures, including those with and without direct experience with this procedure.

Results

There is currently no evidence for head-to-head comparison between paclitaxel-coated balloon dilation and direct vision internal urethrotomy (the most common treatment method for bulbar recurrent urethral stricture in Ontario) or between paclitaxel-coated balloon dilation and surgical urethroplasty (the gold standard treatment). We identified 1 randomized controlled trial that compared outcomes of treatment with paclitaxel-coated balloon with other endoscopic methods (ROBUST III trial). This trial used Kaplan-Meier analysis and reported a statistically significant difference in freedom from repeat intervention at 1 year, favouring the intervention group (GRADE: Low). However, this estimate was likely skewed by the fact that there were participants in the intervention group who failed the treatment but did not undergo reintervention. These cases were excluded (censored) from the analysis, which made the intervention look more effective than it might actually be. Furthermore, outcomes for each of the various endoscopic methods included in the control group were not analyzed individually. Paclitaxel-coated balloon treatment may improve bothersome urinary symptoms and urine flow rate (GRADE: Low). Sexual function was not affected by the treatment in either group (GRADE: Moderate). The rate of hematuria and dysuria during the first month after treatment was higher in the intervention group than in the control group (GRADE: Moderate).

We identified 2 economic studies which found that paclitaxel-coated balloon dilation was potentially cost saving at 5 years compared with usual endoscopic procedures. However, these studies were not directly applicable to the Ontario context. Our economic evaluation from the Ministry of Health perspective found that, compared with usual care over 5 years, paclitaxel-coated balloon dilation could be less costly (mean: −$1,476.44; 95%; credible interval [CrI]: −$3,217.15 to $112.40 per person) and more effective (showing a decrease in the recurrence of urethral strictures at 5 years; mean: 69%; 95% CrI: 68% to 70%). In the reference case analysis, the new treatment was cost-saving about 97% of the time. However, currently published clinical evidence that informed modeling of the effectiveness of this technology was limited and of low quality. In scenario analyses, the cost-effectiveness results were sensitive to changes in the effectiveness of paclitaxel-coated balloon dilation, duration of time horizon, and device cost.

The 5-year budget impact of publicly funding paclitaxel-coated balloon dilation in eligible males is potentially cost saving, with net savings of about $0.74 million from treating 2,747 adult males in Ontario. Assuming a high rate of the procedure uptake from 50% in year 1 to 100% in year 5, we found additional costs of about $0.28 million in the first year of funding and annual savings for the remaining years ranging between $0.02 million and $0.58 million.

The people with bulbar urethral strictures with whom we spoke reported hesitancy about undergoing urethroplasty and viewed paclitaxel-coated balloon dilation favourably due to it being a minimally invasive procedure. Barriers to access included lack of awareness of the procedure, the out of pocket cost when accessing it through a private clinic, and distance from hospitals or clinics performing the procedure.

Conclusions

There is currently no evidence for head-to-head comparison between paclitaxel-coated balloon dilation and direct vision internal urethrotomy or between paclitaxel-coated balloon dilation and surgical urethroplasty. While freedom from reintervention in ROBUST III trial favoured the intervention group, this may have been overestimated. However, paclitaxel-coated balloon dilation may improve urinary symptoms and urine flow rate. The rate of hematuria and dysuria during the first month after treatment was higher in the intervention group than in the control group.

Paclitaxel-coated balloon dilation may be more effective and less costly than usual care for adult males with unsuccessfully treated recurrent and symptomatic bulbar urethral strictures. We estimate that publicly funding paclitaxel-coated balloon dilation in Ontario may result in cost savings of about $0.74 million over the next 5 years. Our economic analysis results remain uncertain and ought to be interpreted with caution because of limitations and low quality of the currently published clinical evidence. People with recurrent bulbar urethral strictures reported viewing paclitaxel-coated balloon dilation favourably because it is minimally invasive, but noted barriers to access.

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Objective

This health technology assessment evaluates the effectiveness, safety, and cost-effectiveness of paclitaxel-coated balloon dilation for adults with recurrent bulbar urethral stricture. It also evaluates the budget impact of publicly funding the technology and the experiences, preferences, and values of people with bulbar urethral stricture.

Background

Health Condition

The male urethra is a tube-like structure that extends from the bladder neck to the meatus (the opening where urine exits the body). It consists of 2 segments: the anterior urethra, which includes bulbar and penile urethra, and the posterior urethra, which is subdivided into the membranous and the prostatic urethra.

Urethral stricture is the abnormal narrowing of a segment of urethra and can develop at any age. Symptoms of urethral stricture may include difficulty urinating, decreased urine stream, incomplete bladder emptying, dysuria, and urinary tract infection. Some of the signs and symptoms of urethral stricture may be similar to other conditions, such as urinary tract infections from other causes or benign prostatic hyperplasia.

Urethral stricture can be caused by infection, sexually transmitted disease, blunt perineal trauma, radiation therapy for prostate cancer, or by iatrogenic interventions such as urethral instrumentation and transurethral procedures. It can also occur after hypospadias or epispadias (a congenital defect in the location of the meatus) repair in childhood, or due to lichen sclerosus (a skin disease that may affect the head of the penis).[1] However, in many cases, it is idiopathic. Urethral stricture requires definitive treatment because it can lead to a urinary tract infection or renal disease.

Tests that are commonly used to diagnose urethral stricture and determine its location, length, and severity include physical examination, imaging studies, cystoscopy, and retrograde urethrogram. Uroflowmetry and post-void residual urine volume (PVR) are also performed at the time of initial investigation to assess the maximum urethral flow and the ability to empty the bladder. The parameters of uroflowmetry include maximum flow rate (Qmax), average flow rate (Qave), and voided volume. The flow rate is measured as the volume of urine voided per second and the Qmax is the maximum value of the urine flow rate measured in milliliters per second. The PVR is the volume of urine left in the bladder when voiding is complete.[2] The International Prostate Symptom Score (IPSS) is also used to assess disease severity and response to therapy. The IPSS scoring system is made up of 7 questions related to voiding symptoms. A score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms, and 20 to 35 indicates severe symptoms.

Clinical Need and Population of Interest

Urethral strictures are associated with a high burden on the quality of life of patients and on health care expenditures. The prevalence of urethral stricture is reported as 229 to 627 per 100,000 men (~0.6%).[3] A large study reported that urethral strictures were in the anterior urethra in 92.2% and in the posterior

urethra in 7.8% of the people seeking treatment for urethral stricture. Within the anterior section, 46.9% were in the bulbar segment, 30.5% in the penile segment, and 9.9% in the bulbar plus penile segments, while 4.9% were panurethral.[1]

The etiology of urethral stricture differs across geographic settings and varies with socioeconomic factors and access to health care. In high-income countries, the most common cause of urethral stricture is idiopathic or iatrogenic interventions, while trauma is the most common cause in low- and middle-income countries, reflecting higher rates of road traffic injuries and inadequate roadway systems in these places.[4]

Current Treatment Options

The core principle for treating urethral stricture is to relieve symptoms and improve quality of life, which requires shared decision-making between the patient and doctor to weigh the risks of various treatments and their potential for long-term efficacy. The first-line treatment of bulbar urethral stricture is an endoscopic procedure. In some clinical practices around the world, endoscopic treatment is performed using a simple balloon or a rigid dilator to dilate the stricture. A more common endoscopic procedure for bulbar urethral stricture is direct visual internal urethrotomy (DVIU),[5] described in more detail below. Urethral stents are no longer recommended for the treatment of urethral strictures due to common and severe stent-related complications.[3]

Urethral Dilation

Urethral dilation is performed with a balloon catheter or a rigid dilator. The goal is to increase the caliber of the narrow part of the urethra.

Use of a rigid dilator is often accompanied by bleeding, suggesting that the urethra is torn while being stretched. Because the procedure is performed in a blinded fashion, it may cause complications, including excessive bleeding, urethral perforation, and false passage. In balloon dilation, a balloon catheter is inserted into the urethra. Inflation of the balloon applies a radial force on the stricture to stretch it. The balloon has less shearing force than the rigid dilator and reduces trauma. It is generally safer because only the narrowed part of the stricture is stretched.[6] Both techniques are associated with a high rate of recurrence. A retrospective study reported a recurrence rate after simple balloon dilation of 50% after 12 months. The median time to recurrence was 6 months.[7]

Direct Visual Internal Urethrotomy

The DVIU endoscopic procedure is usually performed in the operating room and uses a blade or laser to make a longitudinal cut through the stricture under direct vision to widen the lumen. Following the procedure, a bladder catheter is placed for 24 to 72 hours (the patient is typically discharged the same day). The success of the procedure depends on stricture location and length, number of strictures, amount of fibrosis in the surrounding tissues, and number of previous urethrotomies.[8] Intralesional application of antiproliferative agents such as mitomycin C or triamcinolone have been used as adjuncts to DVIU to reduce the recurrence rate by decreasing fibroblast activity and scar tissue formation.[9]

A survey study investigated the patterns of the management of adult male anterior urethral stricture among urology experts from European countries and reported that DVIU was the most frequently chosen method in anterior urethral stricture (79.6% of respondents).[10]

Urethroplasty

Urethroplasty encompasses a multitude of surgical techniques employed to reconstruct the urethra. It is a challenging operation that requires reconstructive expertise, but it is generally well tolerated, with a high rate of success.[11] Urethroplasty is considered the gold standard treatment for anterior urethral strictures of any length and may be offered to the patient as a definitive treatment when the stricture recurs after first-line treatment.[3]

Health Technology Under Review

Adjunctive agents have been used in endoscopic treatment of urethral strictures to prevent or minimize scar tissue formation and reduce stricture recurrence. Scar-modulating drugs used in the treatment of bulbar urethral stricture include colchicine, mitomycin C, tacrolimus, and paclitaxel. These agents have been shown to inhibit inflammation and proliferation of fibroblasts to reduce stricture recurrence.[3] A recent study investigated using paclitaxel-coated balloon as another treatment option. This procedure can be performed with rigid cystoscopy in the operating room or with flexible cystoscopy in the clinic setting.[12]

The technology has been suggested to be used when the stricture recurs after endoscopic treatment and before considering urethroplasty. The paclitaxel-coated balloon is designed to be used for strictures no more than 3 cm in length and should be used only if there is no infection in the urinary tract system.[13] It is available in different diameters (18Fr, 24Fr, 30Fr, and 36Fr) and lengths (3 and 5 cm). Selection of balloon size depends on the lumen diameter and stricture length and needs to allow for a 0.5 to 1 cm overlap of normal tissue on both ends of the stricture. The balloon diameter is 6 to 10 mm, and the drug coating is evenly distributed across the balloon surface at a concentration of 3.5 mcg/mm^2. The drug is released and transfers to the urethral scar tissue once the balloon is inflated. The most commonly used balloon diameter in the bulbar area is 30Fr.[12]

Paclitaxel is a member of taxane family and is one of the most used chemotherapeutic drugs for treatment of various cancers, such as ovarian, breast, and non–small cell lung cancers. It is an antimitotic drug that inhibits cell mitosis and is considered as a cytotoxic and genotoxic drug. Paclitaxel has also been used as an antiproliferative agent for endovascular interventions, and a health technology assessment on paclitaxel drug-eluting stent for peripheral arterial disease was conducted by Health Quality Ontario in 2015.[14]

The risks associated with paclitaxel concentrations in semen and its effect on sperm and spermatogenesis are still unknown. The manufacturer has recommended that, since paclitaxel can be present in semen after treatment with paclitaxel-coated balloon, couples able to conceive should take steps to avoid pregnancy for at least 6 months after treatment.

Regulatory Information

Currently, 1 paclitaxel-coated balloon – Optilume – is approved by Health Canada as a Class II medical device for the treatment of anterior urethral strictures in adult men (license number 101026). The technology was granted European Conformité Européene (CE) mark approval in September 2020 and was also approved by the US Food and Drug Administration in December 2021.

Ontario, Canadian, and International Context

First-line treatment for bulbar urethral stricture may include using a simple balloon or a rigid dilator or DVIU. Direct visual internal urethrotomy is the most used first-line treatment in Ontario for bulbar urethral strictures that are less than 3 cm in length. If the stricture and symptoms recur, urethroplasty may be offered as a definitive treatment. In Ontario, there are about 6 to 10 urologists who have expertise in performing urethroplasty**.**

The paclitaxel-coated balloon has been suggested as an intermediate treatment before offering urethroplasty in people who had at least 1 previous endoscopic treatment. Paclitaxel-coated balloon is currently in use at a few hospitals and private clinics in Ontario and in other provinces of Canada for the treatment of bulbar urethral strictures. At the time of writing, the cost of the device is covered by the hospital's global budget or out of pocket by the patient. Optilume is a single-use device and costs $2,800 per unit (Laborie, Inc., personal communication, June 23, 2025).

The 2020 Canadian Urological Association guidelines on urethral strictures[15] did not specifically include the paclitaxel-coated balloon in their recommendations since the publication of the guidelines preceded publication of the ROBUST III trial. The guidelines recommend that, in men initially presenting with symptomatic urethral strictures of 2 cm or less, DVIU or urethral dilation can be performed prior to offering urethroplasty, but in men with recurrent urethral stricture where endoscopic treatment has failed, urethroplasty should be performed rather than repeating endoscopic treatment because the repeat endoscopic treatment may increase urethroplasty complexity and also increase the rate of recurrence.[15]

The 2023 American Urological Association guidelines[4] made a conditional recommendation that, for treatment of recurrent bulbar urethral strictures of less than 3 cm, surgeons may offer urethral dilation or DVIU, combined with drug-coated balloons (GRADE B recommendation).[*] The guideline also recommends that surgeons offer urethroplasty instead of repeated endoscopic treatment for recurrent anterior urethral strictures after a failed dilation or DVIU.[4]

The National Institute for Health and Care Excellence (NICE) in the United Kingdom developed guidance on Optilume in November 2022, recommending using it as an option to treat recurrent bulbar urethral strictures in adults only if comparative data is collected on patient-reported outcome measures and reintervention rates.[16]

Equity Context

We used the PROGRESS-Plus framework[17] to help explicitly consider health equity in our health technology assessments. PROGRESS-Plus is a health equity framework used to identify population and individual characteristics across which health inequities may exist. These characteristics include place of residence; race or ethnicity, culture, or language; gender or sex; disability; occupation; religion; education; socioeconomic status; social capital; and other key characteristics (e.g., age) that stratify health opportunities and outcomes.[17]

[*]Grade B: moderately confident in the effect estimate; the true effect may be substantially different from the estimate of the effect.

Expert Consultation

We engaged with an expert specialized in the field of urology to help inform our understanding of aspects of the health technology and our methodologies and to contextualize the evidence.

PROSPERO Registration

This health technology assessment has been registered in PROSPERO, the international prospective register of systematic reviews (CRD42024563567), available at crd.york.ac.uk/PROSPERO.

Clinical Evidence

Research Question

What are the effectiveness and safety of paclitaxel-coated balloon dilation compared with endoscopic treatment or urethroplasty for the treatment of adult males with recurrent and symptomatic bulbar urethral stricture?

Methods

Clinical Literature Search

We performed a clinical literature search on June 6, 2024, to retrieve studies published from inception until the search date. We used the Ovid interface in the following databases: MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the National Health Service Economic Evaluation Database (NHS EED).

A medical librarian developed the search strategies using controlled vocabulary (e.g., Medical Subject Headings) and relevant keywords. The final search strategy was peer-reviewed using the PRESS Checklist.[18]

We created database auto-alerts in MEDLINE and Embase, and monitored them until July 21, 2025. We also performed a targeted grey literature search of the International HTA Database, the websites of health technology assessment organizations and regulatory agencies, and clinical trial and systematic review registries, following a standard list of sites developed internally. See Appendix 1 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Randomized controlled trials (RCTs), comparative observational studies, health technology assessments (HTAs), and systematic reviews of RCTs or comparative studies

Exclusion Criteria

- Editorials, commentaries, case reports, conferences abstracts, letters
- Animal and in vitro studies

Participants

Inclusion Criteria

- Adult males with recurrent and symptomatic bulbar urethral stricture ≤ 3 cm in length

Exclusion Criteria

- Urethral strictures caused by benign prostatic hyperplasia

Interventions

Inclusion Criteria

- Paclitaxel-coated balloon catheter for urethral dilation

Exclusion Criteria

- Non–paclitaxel-coated balloon dilation

Comparators

Inclusion Criteria

- Other endoscopic treatments (including various urethral dilation procedures and direct vision internal urethrotomy [DVIU])
- Urethroplasty

Exclusion Criteria

- Non-endoscopic treatment

Outcome Measures

- Reintervention rate for recurrence of urethral stricture
- Time to reintervention for recurrence of urethral stricture
- Change in maximum urinary flow rate (Qmax)
- Change in post-void residual volume (PVR)
- Change in International Prostate Symptom Scores (IPSS)
- Quality of life scores
- Rate of adverse events
- Sexual function
- Effect on semen (infertility, damage to sperm cells, teratogenicity)

Literature Screening

One reviewer screened titles and abstracts using Covidence systematic review management software[19] and obtained the full texts of studies that appeared eligible for review, according to the inclusion criteria. The reviewer then examined the full-text articles of identified studies and selected studies eligible for inclusion. The reviewer also examined reference lists of identified studies and consulted content experts for any additional relevant studies not identified through the search. Citation flow and reasons for exclusion for full text articles are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[20]

The 2 preliminary studies on paclitaxel-coated balloon dilation (ROBUST I and ROBUST II) that investigated the safety and efficacy of paclitaxel-coated balloon dilation before ROBUST III did not meet the eligibility criteria for inclusion in this review because they both were single-arm studies.

Data Extraction

A single reviewer extracted relevant data on study design and characteristics, risk-of-bias items, PICOTS (population, intervention, comparator, outcome, time, and setting), and results.

Equity Considerations

Potential equity issues related to the research question (*or* the use of paclitaxel-coated balloon dilation in adults with bulbar urethral stricture) were not evident during scoping. However, we report the available characteristics of participants in the included studies (e.g., PROGRESS-Plus categories[17]).

Statistical Analysis

We did not conduct a meta-analysis as there was only 1 published study that met our eligibility criteria. Therefore, we provide a narrative summary of the results.

Critical Appraisal of Evidence

A single reviewer assessed risk of bias using the Cochrane risk-of-bias tool for randomized trials (RoB 2)[21] and JBI[22] tools. We evaluated the quality of the body of evidence for each outcome according to the *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) *Handbook*.[23] The body of evidence was assessed based on the following considerations: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The overall rating reflects our certainty in the evidence.

Results

Clinical Literature Search

The clinical literature search yielded 31 citations, including grey literature results and after removing duplicates, published from database inception until June 6, 2024. We did not identify additional eligible studies from other sources, including database alerts (monitored until July 21, 2025). In total, we identified 1 randomized trial and the 2-year follow-up of the same trial that met our inclusion criteria. The results of the 3-year follow-up of the same trial were published after the search date and were identified through the auto-alert. Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the clinical literature search.

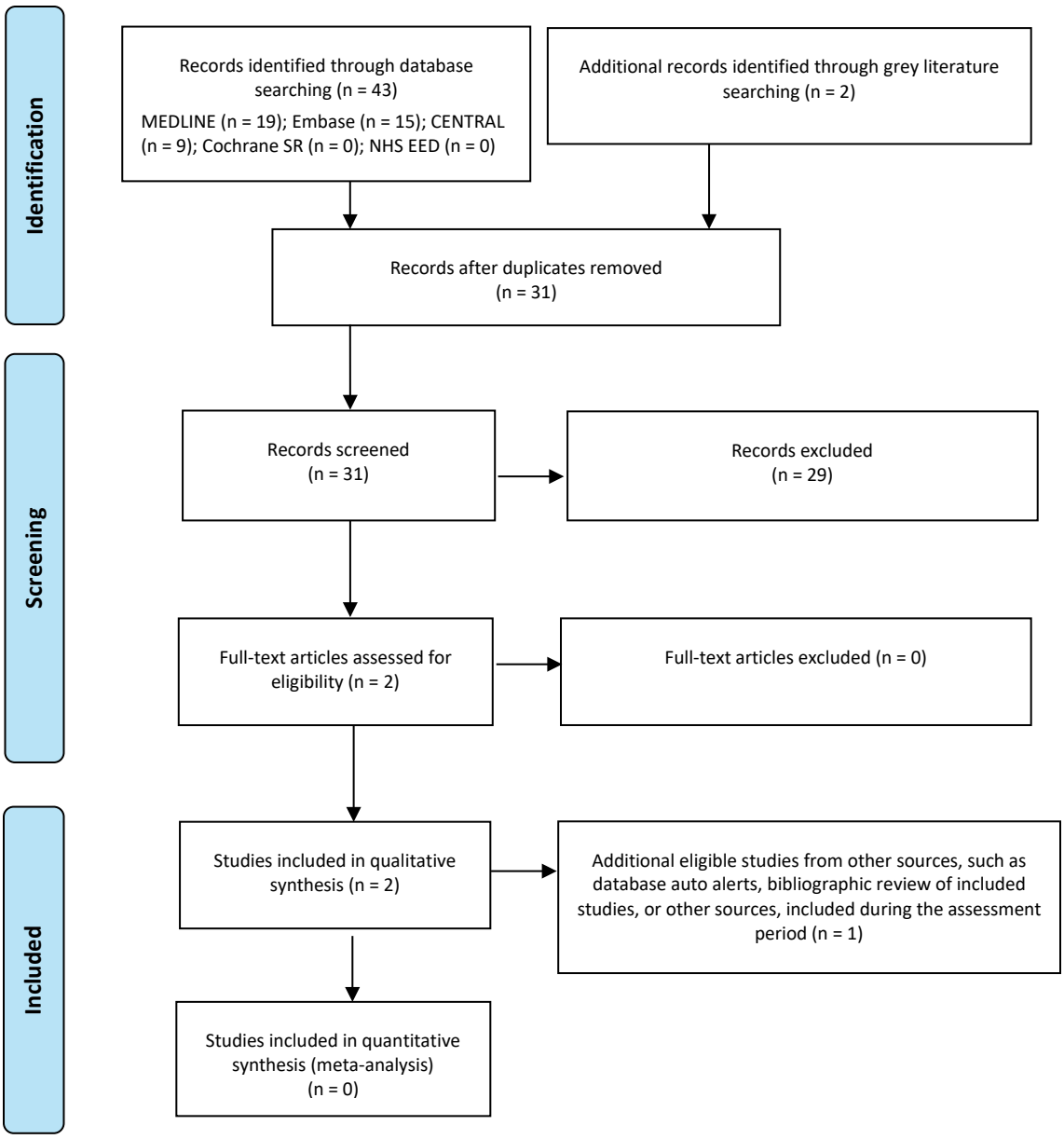

Figure 1: PRISMA Flow Diagram – Clinical Systematic Review

PRISMA flow diagram showing the clinical systematic review. The clinical literature search yielded 43 citations, including grey literature results and after removing duplicates, published between database inception and June 6, 2024. We screened the abstracts of the identified studies and 2 publications from 1 study were eligible for full text review. A third publication from the same trial was identified through auto-alert. In the end, we included the 3 identified publications in the qualitative synthesis.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[20]

Study Design and Characteristics

The ROBUST III trial was an industry-funded phase 3 RCT that enrolled 127 men with recurrent anterior urethral stricture (bulbar stricture: intervention 89.9%, control 95.7%).[24] The study was conducted at 21 American sites and 1 Canadian site (4 patients were enrolled at McGill University Health Centre). The goal of the study was to evaluate the safety and efficacy of paclitaxel-coated urethral balloon dilation in comparison with other endoscopic treatment methods, including dilation of the stricture with a simple (uncoated) balloon or a rigid dilator, or DVIU. Sample size calculation was based on the primary endpoint, which was anatomical success at 6 months post-treatment (defined as the proportion of participants in whom a 16Fr flexible cystoscope or a 14Fr catheter could be passed without trauma). Post-procedural follow-ups were scheduled for 30 days and 3, 6, and 12 months for both groups, and then annually for 5 years for the intervention group only. Therefore, for comparison of outcomes, we report only 1-year outcomes and some related information from the follow-up studies.

For pharmacokinetic investigation, the study included a cohort of 15 non-randomized participants and samples of plasma, semen, and urine were collected from these individuals before and after treatment to measure the amount of the drug in the blood, urine, and semen at different time points.

People who were eligible and were included in the study had anterior urethral strictures of 12Fr or less in diameter and 3 cm or less in length, 2 or more prior endoscopic treatments, IPSS of 11 or higher, and Qmax less than 15 ml per second. Participants who had previous urethroplasty, hypospadias repair, lichen sclerosus, benign prostatic hyperplasia, or unresolved confounding conditions, such as bladder neck contracture or neurogenic bladder, were not included in the study.

Eligible participants were randomized in a 2:1 allocation stratified by prior pelvic radiotherapy (yes vs. no) and prior endoscopic treatments (< 5 vs. ≥ 5). The intervention group contained 79 participants and the control group 48. The mean age of the participants was 58.7 years (SD 15.5 years) in the intervention group and 60.6 years (SD 16 years) in the control group. The mean length of the strictures was 1.7 cm. Participants had an average of 3.6 prior endoscopic procedures for treatment of strictures (intervention: 3.2, control: 4.3). The study was single-blinded, with participants blinded to the treatment they received for 6 months or until another intervention became necessary, while health care providers were aware of participants' treatment assignments. Participants in the control group were allowed to cross over to receive paclitaxel-coated balloon dilation at any time if stricture recurrence was confirmed by a decreased flow rate, a stricture diameter of less than 12Fr measured by retrograde urethrogram, or they experienced recurrent symptoms.

Method of Treatment

In the intervention group, participants received pretreatment dilation with a simple ballon, DVIU, or both. After pretreatment dilation, the paclitaxel-coated balloon was inserted through a cystoscope and was located against the stricture. Then the balloon was inflated and kept inflated for at least 5 minutes to allow complete dilation and drug delivery. The mean time for balloon inflation was 8 minutes and 42 seconds. In the control group, no participant received pretreatment dilation; their method of treatment was based on the conventional method in each centre – simple balloons, DVIUs, and rigid dilators were used in 58.3%, 25%, and 16.7% of participants, respectively. After the procedure, a Foley catheter (12Fr–14Fr) was inserted in the urethra of participants in both treatment groups for 2 to 5 days. Table 1 shows details for the method of treatment in the intervention and control groups.

Table 1: Method of Treatment – Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

	Pre-treatment dilation		Treatment	
Author, year	**PCB**	**Control**	**PCB**	**Control**
Elliott et al, 2022[24]	Simple balloon: 73 (92.4%) DVIU: 4 (5.1%) Both: 2 (2.5%)	None	Paclitaxel-coated balloon: 79 (100%) • 36Fr: 3 (3.8%) • 30Fr: 70 (88.6%) • 24Fr: 6 (7.6%)	Simple balloon: 28 (58.3%) • 30Fr: 11 (23%) • 28Fr: 1 (2%) • 24Fr: 16 (33.3%) DVIU: 12 (25%) Rigid dilator: 8 (16.7%)

Abbreviations: DVIU, direct vision internal urethrotomy; PCB, paclitaxel-coated balloon dilation.

Events Occurring During the Study

In the first year, 2 participants in the intervention group withdrew consent, 1 was lost to follow-up, and 1 died due to intestinal infarction. In the control group, 1 participant withdrew consent.

A urethral lumen test was performed at 6 months in 69 of 79 participants in the intervention group (2 participants had treatment failure, 1 died, 1 withdrew consent, and an additional 6 missed the test) and 31 of 48 participants in the control group (12 crossed over to the intervention group before 6 months, and an additional 5 missed the test).

The open-label phase of the study started after 6 months, and another 12 participants from the control group crossed over to the intervention group. In total, during the first year, 24 (50%) participants in the control group crossed over to the intervention group. Table 2 describes the events that occurred during the first year after treatment and during follow-ups.

Table 2: Events Occurring During the Study: Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

Event	Blinded phase ≤ 6 months	Open-label phase 6–12 mo	2 years (intervention)	3 years (intervention)
Failed urethral lumen test	Intervention: 15 Control: 12	–		
Crossed over to other arm (excluded)	Intervention: 0 Control: 12	Intervention: 0 Control: 12		
Treatment failure (without reintervention)	Intervention: 2 Control: 0	Intervention: 5 Control: 2	8	5
Withdrew consent, lost to follow-up, died, investigator discretion	Intervention: 2 Control: 0	Intervention: 2 Control: 1	7	2
Repeat intervention	Intervention: 2 Control: 18	Intervention: NR Control: NR		
Missed assessment	Intervention: 6 Control: 5	Intervention: 8 Control: 6		
Available for assessment	Intervention: 69/79 Control: 31/48	Intervention: 60/79 Control: 15/48	53/79	45/79

Abbreviation: NR, not reported.

Primary Outcome: Anatomical Success by Urethral Lumen Test

Anatomical success at 6 months was the primary outcome of the study. Success was defined as "the ability to pass a 16Fr flexible cystoscope or a 14Fr rubber catheter through the treated stricture without significant resistance."[24] At 6 months post-treatment, physical examination of the stricture was performed for participants in both groups by passing a 16Fr flexible cystoscope (n = 105) or a 14Fr Foley catheter (n = 3) into the urethra.

In the analysis, participants who received another treatment for the target stricture before 6 months and did not undergo urethral lumen test were counted as failing the lumen test performed at 6 months. This approach contradicted the definition of anatomical success and resulted in an underestimation of anatomical success in the control group (in which 12 participants had crossed over and another 6 had a second treatment, while only 2 participants in the intervention group had another intervention in the first 6 months).

Based on imputation of missing data, the authors reported that 50 of 67 participants (74.6%) in the intervention group and 11 of 41 (26.8%) in the control group passed the urethral lumen test and were stricture-free. A model-based estimate showed a difference of 44.4% (95% CI, 27.6—61.1; $P < .001$) between the intervention and control groups. However, participants who crossed over from the control group to the intervention group had mean IPSS scores of 7.4 and 9.1 at 3 and 6 months, respectively. The Qmax at 3 and 6 months was above the threshold level (< 15 ml/s). Therefore, it is possible that some participants who crossed over did not have bothersome urinary symptoms and the test itself may have prompted additional intervention.

We rated the quality of evidence (GRADE) for the outcome of anatomical success as "Very low," downgrading due to high risk of bias, inconsistency, and lack of clinical applicability, and possible bias in measurement of outcome (see Table A8, Appendix 2).

Secondary Outcomes

Repeat Intervention at 1 Year

The authors did not report the type of repeat intervention participants received.[24] Time to treatment failure, which was a secondary outcome of the study, was also not reported. They used the Kaplan-Meier "time-to-event" analysis to produce an estimate for freedom from repeat intervention. However, in this analysis, there was a considerable difference in the number of censored (excluded) participants in the 2 groups at 1 year (24 in the intervention and 4 in the control). In the intervention group, only 4 participants were eligible to be censored. There were participants in the intervention group who had treatment failure but did not undergo reintervention, as well as some other participants for whom the authors did not provide explanation (possibly those who had failed the urethral lumen test but did not have reintervention); all these were considered "censored" and excluded from the analysis. Therefore, the analysis produced an overestimated result in which the intervention group showed a higher percentage for freedom from repeat intervention (intervention: 83.2%; control: 21.7%; $P < 0.001$). In survival analysis, censoring must be "non-informative" (i.e., unrelated to the event under study) to avoid producing a biased estimate, but most participants in the intervention group who were censored were "informative" and were related to the future risk of the event under study.

There was also disparity in the reintervention options. While the control group had the option to cross over to the intervention group (which was another endoscopic treatment), the option for the

intervention group was likely limited to urethroplasty since they previously failed several endoscopic treatments. There may be multiple explanations for the lower rate of reintervention in the intervention group, including patient preference toward not undergoing an invasive surgery, comorbidities, access to specialized centres, costs, and long waiting time.

Follow-ups

The 2- and 3-year follow-ups are reported for the intervention group only. A total of 26 participants were censored (excluded) in the analysis for freedom from reintervention in the second year. This included an additional 15 participants (8 who had treatment failure in the second year but didn't undergo repeat intervention, 3 who withdrew their consent, 1 who was lost to follow-up, 1 death due to lung cancer, and 2 who were removed from the analysis at the investigator's discretion). Like the first year, the exclusion of participants with treatment failure and no intervention resulted in an overestimation of freedom from repeat intervention in the intervention group. The authors compared the estimate at 2 years for the intervention group with the estimate at 1 year for the control group (77.8% vs. 21.7%) and reported a statistically significant difference (54.2%; 95% CI: 38.7%–69.7%; $P < .001$).[25]

During the third year, 2 participants in the intervention group withdrew consent, and 5 had treatment failure but did not undergo repeat intervention. Therefore, a total of 34 participants were excluded from the analysis. Through 3 years, a total of 20 participants in the intervention group had treatment failure.[26] The authors reported freedom from repeat intervention as 71.9%, with a 50% difference between this estimate and the 1-year estimate for the control group.

We rated the quality of evidence (GRADE) for the outcome of repeat intervention as "Low," downgrading due to high risk of bias, inconsistency, and lack of clinical applicability (see Table A8, Appendix 2).

Voiding Functions

The investigators measured Qmax and PVR before and after treatment. Generally, a Qmax of 15 ml/s or more with a bell-shaped curve is considered normal, but there is no consensus on the threshold value of PVR that would be considered elevated. In general, in adult males, a PVR of less than 100 mL is considered normal.[27]

For these outcomes, the study used multiple imputation method for missing data. For participants who underwent repeat intervention, the study used the participants' worst observed value for Qmax and PVR.

After treatment, both groups showed improvement in Qmax from baseline to 30 days. At the 3-month visit, the Qmax started to decline in the control group and a gradual decline was observed until the 1-year visit, when its value became close to the baseline value. In the intervention group, although a slight decrease was observed at the 6-month and 1-year visits compared to 30 days, its value was double the baseline value throughout all visits. The authors did not report a statistically significant difference between the 2 groups at different time periods up to the 1-year assessment.

Before treatment, the mean PVR was numerically higher in the control group (133.8 ± 155 vs. 109.8 ± 116.9 in the intervention group), but significance for this difference is not reported. Both groups showed improvement in PVR from baseline to 30-day assessment. The improvement in the control group started

diminishing at 3- and 6-months assessment and its value at 1 year was about the same as before treatment. In the intervention group, the PVR was fluctuating during each assessment. The authors did not report a statistically significant difference between the 2 groups at different time periods up to the 1-year assessment. Table 3 shows Qmax and PVR at different assessment intervals and Figure 1 shows Qmax at different time periods.

Table 3: Voiding Functions – Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

	Qmax, ml/s, mean (SD)[a]		PVR, ml, mean (SD)[a]	
Author, year	**PCB**	**Control**	**PCB**	**Control**
Elliott et al, 2022[24]	**Baseline:** 7.6 (3.4)	**Baseline:** 7.4 (3.5)	**Baseline:** 109.8 (116.9)	**Baseline:** 133.8 (155.1)
VanDyke et al, 2024[25]	30 d: 18.3 (9.1)	30 d: 15.8 (8.5)	30 d: 75.6 (86.2)	30 d: 79.1 (87.3)
Srikanth et al, 2025[26]	3 mo: 18.6 (10.9)	3 mo: 13.3 (9.3)	3 mo: 103.4 (134.4)	3 mo: 113.4 (124.2)
	6 mo: 16.6 (8.9)	6 mo: 11.1 (7.6)	6 mo: 73.1 (117.7)	6 mo: 141.4 (194.1)
	1 y: 15.5 (9.0)	1 y: 7.6 (4.0)	1 y: 94.6 (121.8)	1 y**:** 181.5 (201.7)
	2 y: 12.6 (7.6)		2 y: 91.9 (105.8)	
	3-y: 10.6 (5)		3-y: NR	

Abbreviations: NR, not reported; PCB, paclitaxel-coated balloon dilation; PVR, post-void residual volume; Qmax, maximum flow rate.
[a]Year 1 data from Elliot et al; year 2 from VanDyke et al; year 3 from Srikanth et al.

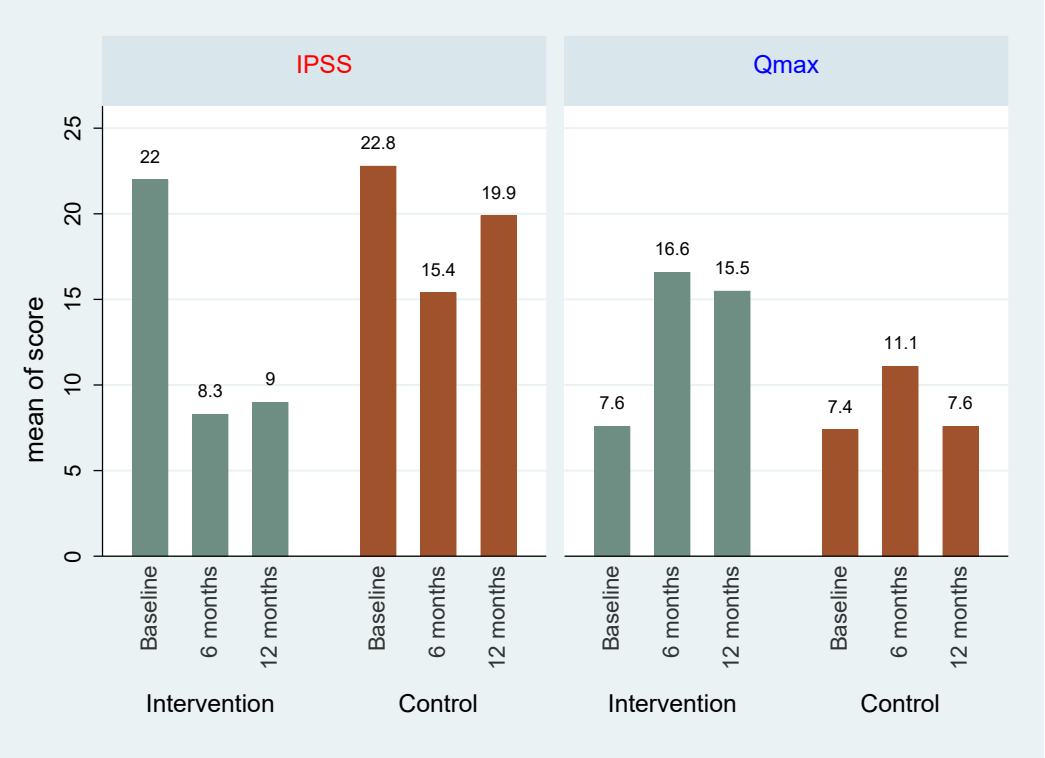

Figure 2: IPSS and Qmax: Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

Bar graph comparing symptom scores (IPSS) and urine flow rates (Qmax) for people receiving paclitaxel-coated balloon dilation ("Intervention") versus other endoscopic treatments ("Control") at baseline, 6 months, and 12 months. Overall, the intervention group showed greater and more sustained improvements in both symptoms and urine flow than the control group.
Abbreviations: IPSS, International Prostate Symptom Scores; Qmax, maximum flow rate.

We rated the quality of evidence (GRADE) for voiding outcomes as "Low," downgrading because of risk of bias and inconsistency (Table A8, Appendix 2).

Voiding Symptoms and Associated Quality of Life

The study used the IPSS, which is a self-administered questionnaire to obtain patient reported data on their voiding symptoms. The IPSS includes 7 questions covering frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying, and urgency, with the severity of the symptom rated on a scale of 0 to 5.[28] Total score shows the overall severity of the condition, where scores of 0 to 7 are considered mild, 8 to 19 moderate, and 20 to 35 severe.[29]

The questionnaire also includes 1 question related to the effect on quality of life due to the bothersome voiding symptoms (IPSS-QOL). This question asks the participants how they would feel if they were to spend the rest of their life with the voiding condition they presently have. Patients can choose 1 of the 7 options provided: delighted, pleased, mostly satisfied, mixed, mostly dissatisfied, unhappy, terrible.[29]

Both groups showed improvement in IPSS and IPSS-QOL from baseline to 30 days. In the intervention group, the improvement observed at 30 days was sustained throughout the assessment period, but in the control group, scores started gradually increasing. The authors did not report a statistically

significant difference between the 2 groups for IPSS or IPSS-QOL. Results of the assessment at different time points are shown in Table 4.

Table 4: IPSS and IPSS-QOL – Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

	IPSS, mean (SD)[a]		IPSS-QOL, mean (SD)[a]	
Author, year	**PCB**	**Control**	**PCB**	**Control**
Elliott et al, 2022[24]	**Baseline:** 22 (6.8)	**Baseline:** 22.8 (7.0)	**Baseline:** 4.5 (1.3)	**Baseline:** 4.7 (1.2)
VanDyke et al, 2024[25]	30 d: 7.6 (5.7)	30 d: 9.5 (7.4)	30 d: 1.7 (1.4)	30 d: 2 (1.6)
Srikanth et al, 2025[26]	3 mo: 7.4 (5.8)	3 mo: 12.4 (9.2)	3 mo: 1.6 (1.4)	3 mo: 2.7 (1.8)
	6 mo: 8.3 (6.2)	6 mo: 15.4 (9.6)	6 mo: 1.7 (1.3)	6 mo: 3.4 (1.8)
	1 y: 9 (7.1)	1-y: 19.9 (7.5)	1-y: 1.9 (1.5)	1 y: 4.0 (1.3)
	2 y: 10.1 (6.7)		2-y: 2.1 (1.3)	
	3-y: 11.6 (7.4)		3-y: NR	

Abbreviations: IPSS, International Prostate Symptom Scores ; NR, not reported; PCB, paclitaxel-coated balloon dilation; QOL, quality of life; SD, standard deviation.

[a]Year 1 data from Elliot et al; year 2 from VanDyke et al; year 3 from Srikanth et al.

We rated the quality of evidence (GRADE) for IPSS and IPSS QOL as "Low," downgrading for risk of bias and inconsistency (Table A8, Appendix 2).

Sexual Function

Sexual function was reported up to the 2-year follow-up examination. The authors used the international index of erectile function (IIEF), a self-administered questionnaire that includes 15 items that examine 5 domains of male sexual function: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.[30] For all domains, a higher score indicates better sexual function. The total score indicates the severity of sexual disfunction, as shown[31]:

- 1–10: severe dysfunction
- 11–16: moderate dysfunction
- 17–21: mild to moderate dysfunction
- 22–25: mild dysfunction
- 26–30: no dysfunction

The study showed that during the first year the overall satisfaction domain of IIEF did not change from baseline in either the intervention or the control group.[24,25] However, scores for both groups were very low at baseline, after treatment, and throughout the year (Table 5).

Scores for the domain of erectile function is reported only for those participants in the intervention group who were sexually active at baseline and shows that treatment with paclitaxel-coated balloon dilation did not affect erectile function (Table 5). The authors did not report a statistically significant difference between the 2 groups for sexual functions. We rated the quality of evidence (GRADE) for sexual function as "Moderate" due to inconsistency (Table A8, Appendix 2).

Table 5: Sexual Function – Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

Author, year	Baseline (SD)	30 days (SD)	3 months (SD)	6 months (SD)	1 year (SD)[a]	2 years (SD)[a]
Elliott et al, 2022[24] VanDyke et al, 2024[25]	**All participants (OS)**					
	PCB: 5.8 (2.9) Control: 6 (3.2)	PCB: 5.9 (2.8) Control: 5.7 (3)	PCB: 6.6 (2.7) Control: 6.1 (3)	PCB: 6.5 (2.8) Control: 6.6 (3.2)	PCB: 6.9 (3) Control: 5.8 (2.7)	NR
	Sexually active (EF)					
	PCB: 20.8 (8.8) Control: NR	PCB: NR Control: NR	PCB: 23.2 (8) Control: NR	PCB: 23 (8.4) Control: NR	PCB: 24.1 (7.4) Control: NR	PCB: 24.2 (7.7) Control: NR

Abbreviations: EF, erectile function; NR, not reported; OS, overall satisfaction; PCB, paclitaxel-coated balloon catheter; SD, standard deviation.
[a]Year 1 data from Elliot et al; year 2 from VanDyke et al.

Safety Outcomes

Adverse Events

Adverse events were reported briefly.[24,25] The authors indicate that hematuria and dysuria occurred more frequently in the intervention group. Most hematuria occurred within the first 30 days after treatment with paclitaxel-coated balloon dilation and were resolved in 10 of 12 participants. The clinical significance of hematuria was not prespecified in trial registration documentation but is described in the published trial as "judged as mild in nature."[24] Other serious adverse events reported were urinary tract infection and aspiration/aspiration pneumonia (Table 6). The authors did not report a statistically significant difference between the 2 groups for adverse events.

Table 6: Adverse Events – Paclitaxel-Coated Balloon Dilation Versus Other Endoscopic Treatments

	Mild, N		Serious, N	
Author, year	**PCB**	**Control**	**PCB**	**Control**
Elliott et al, 2022[24]	Hematuria: 11.4% Dysuria: 11.4%	2.1% 2.1%	Aspiration: 1.3% UTI: 1.3%	Aspiration: 2% UTI: 2%
VanDyke et al, 2024[25]	Hematuria: 13.9% Dysuria: 6.3% Infection: 6.3%	None None None		
Srikanth et al, 2025[26]	No late-onset adverse events			

Abbreviations: PCB, paclitaxel-coated balloon dilation; UTI, urinary tract infection.

We rated the quality of evidence (GRADE) for this outcome as "Moderate" due to inconsistency (Table A8, Appendix 2).

Pharmacokinetic Evaluation

The study enrolled another cohort of 15 non-randomized participants for paclitaxel pharmacokinetic assessments (systemic exposure and paclitaxel concentration in urine and semen). Samples of plasma, urine, and semen were taken from these participants. The authors did not provide information about the participants in this cohort.

Systemic Exposure to Paclitaxel

In this cohort of 15 non-randomized participants, the plasma concentration of paclitaxel at 1 and 3 hours after the procedure were 0.12 and 0.11 ng/ml, respectively. The authors did not report plasma concentration of paclitaxel beyond 3 hours.

We rated the quality of evidence (GRADE) for this outcome as "Very low" due to high risk of bias and inconsistency (Appendix 2, Table A5).

Paclitaxel Concentration in Urine and Semen

The dose of paclitaxel on the balloons that are 30 Fr with 30 mm length is 3,299 mcg, and for balloons that are 30 Fr with 50 mm length it is 5,498 mcg. Most of the paclitaxel was removed through urination within a few days. In 15 non-randomized participants, the level of paclitaxel in urine was 414.4 ng/mL immediately after the procedure, which dropped to 13.8 ng/ml when the Foley catheter was removed. At 30 days, the amount of paclitaxel in urine was below the level of quantification.

In seminal fluid, paclitaxel was detectable in measurable quantities in 9 of 15 (60%), 5 of 13 (39%), and 1 of 12 (8.3%) individuals at 30 days, 3 months, and 6 months, respectively. The drug concentration in semen was 2.99, 0.48, and 0.12 ng/ml at 30 days, 3 months, and 6 months, respectively. Due to the risk of genotoxicity of paclitaxel, the authors recommended that couples able to conceive take steps to avoid pregnancy for at least 6 months after treatment with paclitaxel-coated balloon dilation. Table 7 shows the amount of paclitaxel in urine and seminal fluid in nonrandomized participants.

Table 7: Paclitaxel Concentration in Urine and Semen of Nonrandomized Participants After Treatment

Author, year	Urine concentration, mean (ng/ml)	Semen concentration, mean (ng/ml)
Elliott et al, 2022[24]	Immediately after procedure: 414.4	30 d: 2.99
	At Foley catheter removal: 13.8	3 mo: 0.48
	At 30 d: below the limit of quantification	6 mo: 0.12

We rated the quality of evidence (GRADE) for this outcome as "Very low" due to high risk of bias and inconsistency (Table A8, Appendix 2).

The impact of paclitaxel on the quality of semen and damage to sperm cells, infertility, and teratogenicity are not investigated yet.

Risk of Bias in the Included Study

We assessed the risk of bias for the ROBUST III trial using the RoB 2 tool.[21] We used various domains of this tool for the overall risk of bias assessment for each outcome and determined that the risk of bias was high for repeat intervention, anatomical success, voiding functions, IPSS, and IPSS-QOL, and low for sexual function and adverse events. We used the JBI tool for case series for the outcomes that were assessed only in the 15 non-randomized participants and determined that the risk of bias was high. We provide details for assessing risk-of-bias in Appendix 2.

Ongoing Studies

We are aware of the following ongoing studies that have potential relevance to this review:

- Laser Visual Internal Urethrotomy With Versus Without Paclitaxel Injection. RCT. ClinicalTrials.gov identifier: NCT06123520
- Treatment of Urethral Stricture With Urethral Drug Ball. RCT: drug balloon catheter from Lepu Medical Technology [Beijing] Co., Ltd. ClinicalTrials.gov identifier: NCT05812482
- Role of Paclitaxel in stricture urethra. ClinicalTrials.gov identifier: NCT05678413
- Optilume Registry for Treatment of Stricture of the Anterior Urethra. ClinicalTrials.gov identifier: NCT05479422
- Optilume PoST AppRoval Clinical Evaluation of Andrology ParaMeters. STREAM. ClinicalTrials.gov identifier: NCT05383274

Discussion

Paclitaxel-coated balloon dilation has been introduced into clinical practice to provide an option for patients with recurrent bulbar urethral stricture after initial endoscopic treatment to delay the need for undergoing surgical urethroplasty. Paclitaxel is an adjunctive agent that has the potential to minimize scar tissue formation and reduce stricture recurrence. Initially, 2 single-arm studies (ROBUST I and ROBUST II) evaluated the safety and efficacy of paclitaxel-coated balloon dilation for the treatment of male recurrent short anterior urethral strictures. Since no comparison was made with any other technique, these trials did not meet the eligibility criteria for inclusion in this review. However, a third trial – the ROBUST III trial – investigated the safety and efficacy of paclitaxel-coated balloon dilation in comparison with a combination of other endoscopic techniques (simple balloon, rigid dilator, and DVIU) and was included in this review. Comparative data were reported up to 1 year. Two- and 3-year follow-ups included only the intervention group.

In the ROBUST III trial, the Kaplan-Meier time to event analysis was used to calculate the percentages of participants free from reintervention over time. The study reported a statistically significant difference in freedom from repeat intervention at 1 year, favouring the intervention group. However, the estimate for the control group does not align with the literature. The freedom from reintervention for DVIU in the UK Open trial was 72% at 2 years and a review of patients with urethral stricture who underwent dilation with simple balloon from 2007 to 2021 showed 50% recurrence at a median of 1 year. This discrepancy might be due to the influence of the urethral lumen test in crossing over to the intervention group. Participants who crossed over had a mean IPSS scores of 7.4 and 9.1 at 3 and 6 months, respectively, and Qmax at 3 and 6 months was above the threshold of less than 15 ml/s. This

observation may indicate that some participants in the control group did not have bothersome urinary symptoms but preferred to cross over to receive the alternative treatment after becoming aware of the test result. It is plausible to think that if the urethral lumen test was not part of the trial, there may have been fewer crossovers and repeat interventions in the control group because the test itself might have prompted the need for further intervention in some individuals.

There were participants in the cohort who failed the treatment but did not undergo another intervention and some who may have failed the urethral lumen test with no reintervention. These cases were censored (excluded) in the analysis for freedom from reintervention. This resulted in an unusual difference in the number of censored participants between the 2 groups, with a higher number in the intervention group. This skewed the results and made the intervention look more effective than it might actually be. In the Kaplan-Meier analysis, it is critical that censored data be unrelated to the outcome under study and be "non-informative" (e.g., participants who were lost to follow-up or died), but most censored cases in this analysis were related to future risk of the event under study (informative). These cases were mostly in the intervention group; thus, censoring these participants biased the estimate in favor of the intervention group.

The 2 groups also had very different options for reintervention, which may have impacted their ability or willingness to undergo reintervention after experiencing treatment failure. While participants in the control group were allowed to cross over to the intervention group, which was another endoscopic treatment, the options for intervention group were likely limited to surgical urethroplasty since they already had failed several prior endoscopic treatments. Many factors can influence the probability of undergoing surgical urethroplasty, such as access to specialized centers, waiting time that could be beyond the study duration, health status, and cost.

The post-treatment improvement in urinary flow rate (Qmax) and IPSS observed in the 2 groups during the first year were better sustained in the intervention group than in the control group, but the significance of this observation is not reported. It is not clear whether the improvement in urinary outcomes in the intervention group was because of the drug that was delivered to the stricture or a combination of predilation treatment and subsequent use of the balloon for drug delivery that was kept inflamed for a mean of about 9 minutes. In the ROBUST III trial, stricture was predilated in the intervention group but not in the control group, which might be a confounding factor favouring the intervention group.

Pharmacokinetic assessments were investigated only in a nonrandomized group of 15 participants, which showed systemic exposure with small amounts of the drug in the plasma in the first few hours, but the level of the drug in the plasma beyond 3 hours is not reported. The drug was excreted through the urine in a high concentration immediately after the procedure and most of the remaining drug was excreted within a few days after the procedure. At 30 days post treatment, its level in the urine was below quantification.

Paclitaxel was present in semen in 60% of these individuals at 30 days and was still detected in 8% of participants at 6 months post-treatment. Since paclitaxel is a cytotoxic and genotoxic drug, the study authors recommended that couples able to conceive take steps to avoid pregnancy for at least 6 months after treatment with paclitaxel-coated balloon dilation because the possibility of adverse effects on the fetus is not yet known.

Equity Considerations

A potential equity issue related to our research question and the use of paclitaxel-coated balloon dilation to treat urethral stricture is the possibility of paclitaxel affecting semen quality, sperm cells, and testicular function. Currently, a post-market study (Optilume post-approval clinical evaluation of andrology parameters [STREAM]: NCT05383274) is underway, having enrolled 34 participants in the United States, aged 22 to 65 years. The study authors plan to conduct follow-up assessments at 30 days and at 3, 6, and 12 months post-treatment to evaluate lower urinary tract symptoms, sexual function, and voiding function. Semen quality parameters will be assessed at baseline and at 3 and 6 months post-treatment. Participants with an abnormal semen quality at the 6-month assessment will have an additional assessment at 12 months post-treatment and periodically thereafter until results return to normal.

Strengths and Limitations

This review has several limitations. It was based on only 1 single-blinded industry-funded randomized controlled trial, where surgeons and investigators were aware of the participants' assignment and participants were blinded to the treatment assignment for 6 months only. The study had a 1-year follow-up for both groups and 2- and 3-year follow-ups for the intervention group. The safety outcomes related to the effect on the quality of semen and damage to sperm cells, infertility, and teratogenicity are not yet available.

We did not find any study that compared paclitaxel-coated balloon with DVIU alone, which is a technique that is performed more frequently than dilation with simple balloon or rigid dilator. The ROBUST-III trial considered all 3 endoscopic alternatives (simple balloon, rigid dilator, DVIU) together in the control group. In addition, the technology is a balloon that is coated with an adjunct drug, but we did not have any studies on its comparative effectiveness against other adjunct drugs that are used in endoscopic treatment of the urethral stricture.

The strength of our review is that we clearly addressed issues in the study analytical method that influenced the outcome of freedom from reintervention, and were able to extract a meaningful interpretation of the results.

Conclusions

- There is no evidence for head-to-head comparison between paclitaxel-coated balloon dilation and DVIU, which is the most common treatment method for bulbar urethral stricture in Ontario
- There is no evidence for head-to-head comparison between paclitaxel-coated balloon dilation and surgical urethroplasty
- A Kaplan-Meier analysis from 1 trial reported a statistically significant difference in freedom from repeat intervention at 1 year, favouring the intervention group (GRADE: Low). However, this estimate may be overestimated due to censoring "informative" participants, which favoured the intervention group
- Freedom from reintervention in the control group may have been influenced by the urethral lumen test and does not align with the estimates reported in other studies

- Anatomical success in the control group may be underestimated due to the addition of participants who had repeat intervention without performing a urethral lumen test (GRADE: Very low)
- Although this treatment improves bothersome urinary symptoms (IPSS) and urine flow rate (Qmax), no *P* value for the difference between this endoscopic method and other endoscopic methods is reported (GRADE: Low)
- Treatment with paclitaxel-coated balloon causes more hematuria and dysuria during the first month compared with other endoscopic methods (GRADE: Moderate)
- Treatment with paclitaxel-coated balloon does not affect sexual function (GRADE: Moderate)
- Effect on semen (infertility, damage to sperm cells, teratogenicity) is not currently known

Economic Evidence

Research Question

What is the cost-effectiveness of paclitaxel-coated balloon dilation compared with endoscopic management or urethroplasty for the treatment of adult males with recurrent and symptomatic bulbar urethral strictures?

Methods

Economic Literature Search

We performed an economic literature search on September 23, 2024, to retrieve studies published from database inception until the search date. To retrieve relevant studies, we developed a search using the clinical search strategy with an economic and costing filter applied.

We created database auto-alerts in MEDLINE and Embase and monitored them until August 13, 2025. We also performed a targeted grey literature search following a standard list of websites developed internally, which includes the International HTA Database and the Tufts Cost-Effectiveness Analysis Registry. See Clinical Literature Search, above, for further details on methods used. See Appendix 1 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Studies published since inception
- Cost–utility, cost-effectiveness, cost–benefit, cost–consequence or cost-minimization analyses

Exclusion Criteria

- Narrative or systematic reviews, non-comparative costing (feasibility) studies or cost-of-illness studies, letters/editorials, case reports, commentaries, abstracts, posters, unpublished studies

Population

Inclusion Criteria

- Adult males with recurrent and symptomatic bulbar urethral stricture ≤ 3 cm in length

Exclusion Criteria

- Urethral strictures caused by benign prostatic hyperplasia

Interventions

Inclusion Criteria

- Paclitaxel-coated balloon catheter for urethral dilation

Exclusion Criteria

- Other types of coated balloon catheter (non-paclitaxel coating) for urethral stricture dilation
- Optilume BPH (paclitaxel-coated balloon catheter BPH) for prostatic urethra

Comparators

Inclusion Criteria

- Endoscopic management (including various urethral dilation procedures and direct vision internal urethrotomy [DVIU])
- Urethroplasty

Exclusion Criteria

- No treatment

Outcome Measures

- Costs
- Health outcomes (e.g., rate of recurrence or reintervention due to recurrence, quality-adjusted life-years [QALYs])
- Incremental costs
- Incremental effectiveness
- Incremental cost-effectiveness ratios – ICERs (expressed as an additional cost per a recurrence or reintervention averted, or per 1 QALY gained)

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[19] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion. The reviewer also examined reference lists and consulted content experts for any additional relevant studies not identified through the search.

Data Extraction

We extracted relevant data on study characteristics and outcomes to collect information about the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, analytic technique, perspective, time horizon, population, intervention[s], comparator[s])
- Outcomes (e.g., health outcomes, costs, incremental cost-effectiveness ratios)

Study Applicability and Limitations

We determined the usefulness of each identified study for decision-making by applying a modified quality appraisal checklist for economic evaluations originally developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[32] The NICE checklist has 2 sections: the first is for assessing study applicability and the second is for assessing study limitations. We modified the wording of the questions of the first section to make it specific to Ontario. Using this checklist, we assessed the applicability of each study to the research question (directly, partially, or not applicable). Next, we assessed the limitations (minor, potentially serious, or very serious) of the studies that we found to be applicable.

Results

Economic Literature Search

The economic literature search yielded 6 citations, including grey literature results and after removing duplicates, published from database inception until September 23, 2024. We did not identify additional eligible studies from other sources, including database alerts (monitored until August 13, 2025). In total, we identified 2 English-language articles that met our inclusion criteria.[13] Figure 3 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the economic literature search.

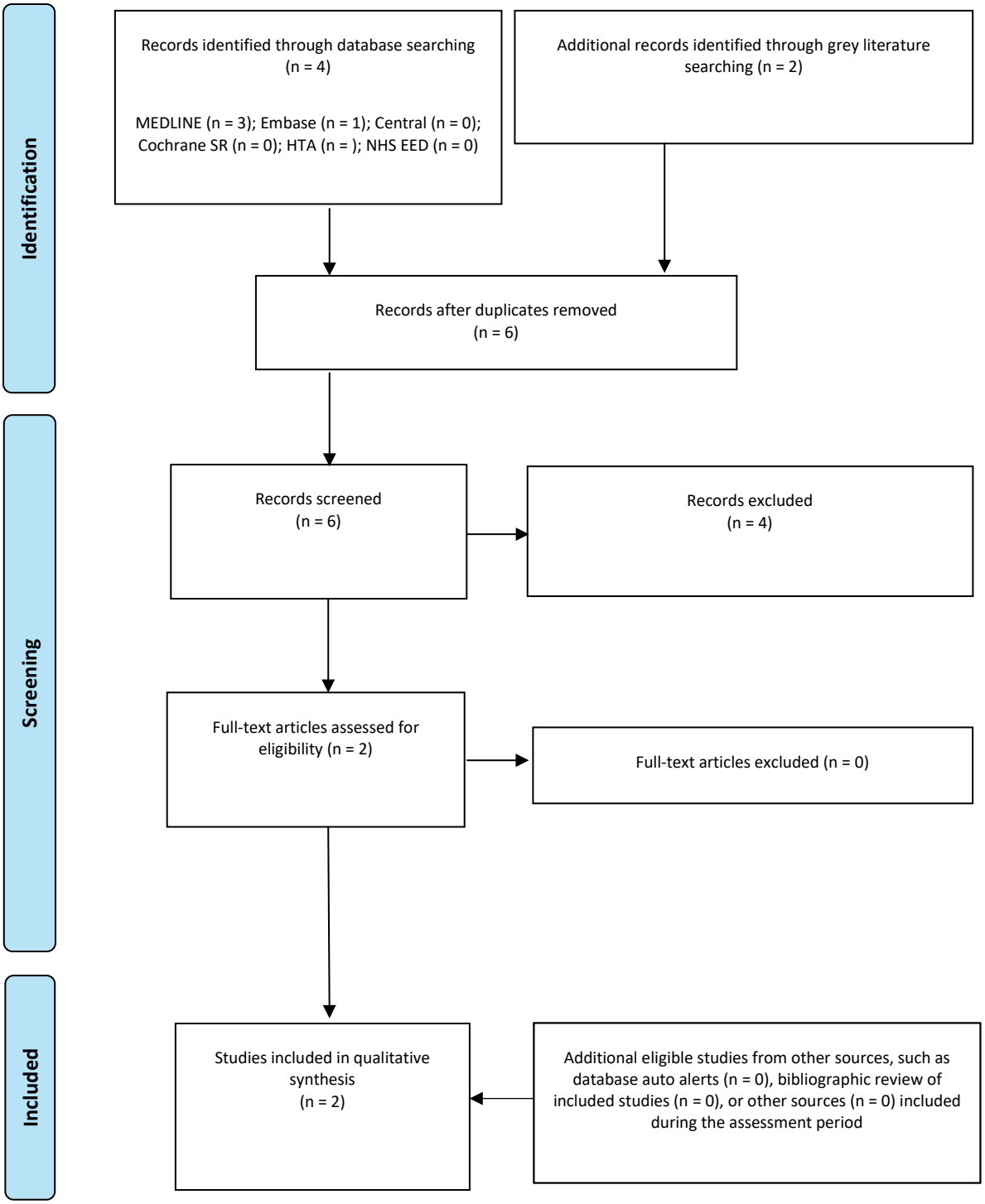

Figure 3: PRISMA Flow Diagram – Economic Systematic Review

PRISMA flow diagram showing the economic systematic review. The economic literature search yielded 6 citations, including grey literature results and after removing duplicates, published between database inception and August 13, 2025. We screened the abstracts of the 6 identified studies and excluded 4. We assessed the full text of 2 English-language articles[33,34] and included both articles in the qualitative synthesis.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[20]

Overview of Included Economic Studies

Table 8 presents methods and results of the 2 included economic studies[33,34] assessing the Optilume (paclitaxel-coated balloon catheter) for urethral dilation and treatment of recurrent bulbar urethral strictures of 3 cm or less in males. The first study is a 2022 NICE External Assessment Center (EAC) MTG73 evaluation, including the manufacturer's (Laborie Medical Technologies; hereinafter, the company) initial submission and subsequent analyses done by both the company and EAC.[33] The second is a primary economic study published in 2023[34] presenting a portion of the 2022 manufacturer's submission to the NICE medical technologies advisory committee (MTAC).[33] These 2 publications were based off the same economic model; hence, in the section below, we elected to summarize the 2022 NICE-EAC evaluation[33] because it comprehensively reported all analyses, including changes to the company's initial assumptions and cost inputs, as well as differences in the results between the initial and subsequent (EAC's) analyses.

Review of Methods

Analysis Design: Study Type, Perspective, Time Horizon, and Discounting

The economic evaluation included model-based cost-consequence analyses that were done from the UK's National Health Services and Personal Social Services (NHS/PSS) perspective (i.e., public payer). The model reflected a clinical and treatment pathway of the recurrent urethral stricture disease and accounted for changes in health outcomes and costs over a 5-year horizon in the base (reference) case. Costs were discounted at a rate of 3.5% in the base case, concurring with the NICE method guidelines.[35]

PICO: Population, Intervention, Comparator, and Outcomes

The population of interest included adult males with recurring bulbar urethral strictures of 3 cm or less who continued to experience bothersome urinary symptoms because they failed 1 or more standard endoscopic procedures, such as various types of urethral dilation or DVIU. For the economic analysis, the base case mean age of the study cohort was assumed to be 59 years (range: 44–74 years), reflecting that of the ROBUST III randomized controlled trial (RCT) participants.[24] Exclusion criteria were related to people who had contraindications to paclitaxel, such as hypersensitivity to paclitaxel or immunocompromised diseases.

The intervention was an endoscopic minimally invasive surgical procedure with the paclitaxel-coated balloon device, which has a proprietary circumferential coating of the anti-fibrotic and anti-proliferative medication paclitaxel. In the procedure, the paclitaxel-coated balloon catheter is passed over a guidewire through the urethra of the penis. When the balloon is in position across the stricture and is inflated, the paclitaxel adheres to the urethra luminal wall.[33] The aim of this process is to prevent new tissue growth as well as scarring and, consequently, recurrence of the urethral stricture disease. Based on expert consultation published in the NICE report,[33] the paclitaxel-coated balloon catheter would not be proposed as the first-line endoscopic treatment in incident cases; rather it would be used in people who become symptomatic because of stricture recurrence. In this way, the need for an anastomotic or augmented urethroplasty, which is a complex invasive surgery requiring general anesthesia and a 1- to 2-day hospital stay, could be delayed. UK experts also indicated that the use of paclitaxel-coated balloon catheter for the urethral stricture treatment could depend on patient preference. The experts consulted by NICE also acknowledged a potential for re-use of the paclitaxel-coated balloon catheter for urethral

dilation after the first unsuccessful treatment despite lack of published evidence on the effectiveness of this device for retreatment of the urethral stricture.

The EAC's analysis[33] assumed that paclitaxel-coated balloon dilation was a day-case procedure (100%), following expert advise that this procedure should only take place in an inpatient setting because it would require sedation in addition to local anesthesia. This is to ensure patient's comfort and stillness while also enabling precise and accurate placement of a balloon catheter. This change in the procedure setting was a major difference from the initial company's analysis, which assumed 50% day-case and 50% outpatient treatment, resulting in more cost savings due to decreased use inpatient stay and theater (operating room) time.

The current practice for the treatment of urethral strictures includes a mix of 2 types of minimally invasive endoscopic procedures – urethral dilatation (various types) and DVIU – typically used as first-line or repeated treatment options in the UK for urethral strictures less than 3 cm in length. The use of this combination was supported by the experts consulted by NICE[33]; it was also justified by the findings of the clinical evidence and guidelines,[33] which showed no statistically significant difference between the success rates of urethral dilation and DVIU at 24 months follow-up.[15,36] In addition, use of self-catheterization was considered in a chronic stricture state, which represented an unsuccessful outcome following multiple endoscopic procedures.

Urethroplasty (anastomotic or augmented) is a complex, invasive inpatient surgery that was considered as a possible treatment option in the clinical treatment pathway, following a first unsuccessful usual care endoscopic or paclitaxel-coated balloon dilation procedure. The analyses[33] accounted for the chance of adverse effects associated with urethroplasty, including infection, bleeding, erectile dysfunction discomfort, fistula formation, and perioral numbness (when a graft is required for augmentation). Urethroplasty was also examined as a main comparator to the paclitaxel-coated balloon dilation procedure in a scenario analysis.

The main outcome was the difference in total costs between paclitaxel-coated balloon dilation and standard-of-care pathways at 5 years after treatment. The estimates of total costs accounted for the effectiveness data for 2 compared options on health outcomes such as stricture recurrence, procedure-related adverse events, and retreatment with and success of urethroplasty. In the base case, *recurrence rates were based on submitted (but unpublished) data*: the rate was defined by the International Prostate Symptom Score (IPSS) questionnaire score improvement of 30% or greater at 1 year.[33] Additional scenarios considered the published rates of anatomical stricture at 6 months and the proportion of patients retreated after 1 year. In addition to costs, the authors estimated a total number of repeat procedures over 5 years as a separate cost-consequence outcome, but no effort was made to examine further the cost-effectiveness of the paclitaxel-coated balloon dilation procedure. The ROBUST III trial[24,33] reported changes (improvement) in disease-specific quality of life via a limited assessment of patient's quality of life by using 1 (single) question on the IPSS (IPSS Q8). However, no investigation of changes in health-related quality of life by a recommended instrument (e.g., EQ-5D) or estimation of QALYs was done.

Analytic (Modeling) Technique, Model Inputs, and Statistical Analyses

A Markov (state-transition) modeling technique was used to simulate the clinical treatment pathway of recurrent urethral strictures in an adult cohort of males, accumulating costs on a monthly cycle basis over 5 years in the reference case. The model was created by the company and was accepted as

appropriate by the EAC.[33] The simulation started with paclitaxel-coated balloon dilation or endoscopic management, a temporary (short-term) health state that accounted for the initial procedure-related costs and adverse events.

In the next model cycle, the cohort transitioned to an *asymptomatic health state ("cured"*), reflecting no symptoms of urethral strictures. The cohort could reside in this state for the rest of the time, or if the symptoms resumed, it transitioned into a *symptomatic health state ("recurrence"*), in which it experienced the urethral stricture symptoms. People in this state were followed up by a physician for the rest of the time, without being treated with any surgical procedure but with a possibility of self-catheterization. Alternatively, they were retreated with either of the following 2 options:

- Endoscopic procedure with the paclitaxel-coated balloon catheter only (the second paclitaxel-coated balloon catheter dilation procedure) in the base case (note: a mix of the endoscopic methods – paclitaxel-coated balloon dilation or usual care procedures used in EAC's scenario)
- Urethroplasty

After completing the second procedure, the cohort transitioned to either an *asymptomatic* or a *symptomatic health state*, with a possibility of another retreatment in the case of recurrence with usual care endoscopic management, paclitaxel-coated balloon dilation, or urethroplasty. People previously treated with urethroplasty were retreated with either paclitaxel-coated balloon dilation or another urethroplasty. From any of the above-mentioned Markov health states, over the time horizon, a portion of the cohort could die from an accident or disease, moving to the absorbing *dead state*. The procedure-specific mortality was not separately modeled but was part of the background mortality.

The model inputs included the effectiveness, safety, and costs of paclitaxel-coated balloon dilation, usual endoscopic, and urethroplasty procedures. Model assumptions and parametrizations were based mostly on data from a US multicentre comparative ROBUST III RCT comparing paclitaxel-coated balloon dilation and endoscopic management (dilation or DVIU) over 12 months,[24] and a UK open-label (OPEN) RCT comparing urethroplasty and DVIU over 24 months in adult males with recurrent bulbar urethral stricture.[37,38]

Effectiveness and Safety Model Inputs

The recurrence of a urethral stricture after the first procedure was estimated from the monthly transition probabilities in the ROBUST III trial, which compared improvement in IPSS (≥ 30% at 12 months) with paclitaxel-coated balloon dilation versus endoscopic management (monthly probabilities based on unpublished data: 2.6% vs. 16.3%, respectively, calculated from 26.9 % vs. 88.1% recurrence rates at 12 months).[24] A constant rate of recurrence was simulated over the time horizon, an assumption that was adopted from the economic study by Pickard et al,[38] which was accepted by the EAC as a conservative assumption (given that a greater number of repeats could be observed with the comparator in reality).

Uptake of the next (second) procedure was assumed from the distribution of the different available treatments provided in the OPEN trial[37,38]; namely, 90% patients were assumed to be retreated and 10% had no further surgical treatment.[38] The distribution spread for re-treatment options was 70% versus 30% for the urethroplasty versus endoscopic management/paclitaxel-coated balloon dilation, respectively.[37,38]

Monthly probabilities for retreatment with any of these procedures were estimated by accounting for the procedure-related waiting time (about 48 days for the endoscopic management and 90 days for the urethroplasty). The effectiveness of treatment with paclitaxel-coated balloon dilation after the second or repeated procedures was assumed to be the same as for the first one, despite little available evidence. The recurrence of urethral strictures after urethroplasty was estimated from the OPEN RCT (0.95% per month, calculated from the reported 20.4% at 24 months).[37,38]

Adverse events at 1 year after paclitaxel-coated balloon dilation and usual care procedures and at 2 years after urethroplasty were estimated from the ROBUST III and OPEN RCTs and included hematuria, urinary tract infection, wound infection, readmission to hospital and urinary retention with emergency admission. The EAC's analysis recognized that hematuria events occurring with the paclitaxel-coated balloon catheter were classified as mild, resolving within 30 days.[33]

Cost Inputs

Total costs were estimated in 2019/20 GBP.[34] They included a 1-time procedure and post-procedure-related costs and monthly incurred health state costs.[33]

- The cost of the Optilume device was £1,350 and the cost of the paclitaxel-coated balloon dilation procedure was about £1,067 (the company's initial estimate of £635 was changed by the EAC), summing up to a total of £2,418. These costs included the cost of annual consumables (£1) and cost of surgical doctor training per patient (£2.62 by the EAC vs. £8.53 initially assumed by the company, accounting for staff time for training, including 4-hour in-dept doctor training by their supervisors that followed a basic free-of-charge training provided by the company). On top of the paclitaxel-coated dilation procedure cost, there were additional costs such as:
  - Pre-dilatation cost of £20.36[33]
  - Post-procedure use of a standard (Foley) urethral catheter, requiring a return visit to the hospital for catheter removal. Although the catheter cost was likely minimal, it was not clear if it was accounted for in the cost of the follow-up clinic visit
- The total estimated cost of usual endoscopic procedures was about £1,196 per person (including the procedure and consumables costs)
- The total estimated cost of the urethroplasty was about £4,761 per person
- The analysis included procedure-related costs for adverse events and monthly-incurred costs for the asymptomatic health state (including 2 GP visits) and for the symptomatic/recurrent health state (including 4 GP visits for the whole cohort), and intermittent self-catheterization for 16.8% of the cohort members

Statistical Analyses: Reference Case and Sensitivity Analyses

Three methods for sensitivity analysis were performed to address parameter, method, and decision uncertainty[33]:

- One-way deterministic sensitivity analyses for all model inputs (results were presented using a tornado diagram)

- Scenarios addressing the use of urethroplasty as a comparator, and changes in the baseline discount rate (range: 2%–4%) and in the duration of the time horizon (1, 10, and 20 years)
- Three 2-way sensitivity analyses, including changes in the 2 parameters described for each analysis at the same time:
  - Monthly probabilities of recurrence with endoscopic management and with paclitaxel-coated balloon dilation
  - Costs of the paclitaxel-coated balloon dilation procedure (excluding device) and endoscopic management procedures
  - Probabilities of urethroplasty following endoscopic management/paclitaxel-coated balloon dilation and another urethroplasty following initial urethroplasty
- Probabilistic analysis that involved setting up the probabilistic distributions for model parameters and running 1,000 simulations to estimate the probability of cost-saving with paclitaxel-coated balloon dilation versus usual care.

Summary of Findings

Reference Case Results

The cost-consequence analyses by the EAC and company consistently showed that treating recurrent male anterior bulbar strictures of less than 3 cm in length with paclitaxel-coated balloon dilation done as a day-case procedure 100% of the time yielded cost savings of about £1,877 (EAC) or £2,502 (company) per person at 5 years (in 2019/20 GBP, Table 8), compared with a mix of usual care endoscopic procedures (urethral dilation and DVIU).[33] At 5 years, treatment with paclitaxel-coated balloon dilation resulted in a total mean discounted cost of £7,249 or £6,620 (EAC or company, respectively) per person, corresponding to the usual care mean cost of £9,126 or £9,122 per person (EAC or company, respectively).

These decreases in the total mean costs were caused by a lower recurrence of urethral strictures with paclitaxel-coated balloon dilation; hence, fewer repeated procedures and less need for urethroplasty over 5 years (paclitaxel-coated balloon dilation vs. usual care: 1.11 vs. 2.31 – a mean reduction of 1.20 procedures per person, where the recurrence rate was defined by the reference case as a ≥ 30% improvement in IPSS).[33]

The downstream cost savings with paclitaxel-coated balloon dilation offset its high initial procedure cost, as shown by estimated cost differences for the following cost components (differences over 5 years between paclitaxel-coated balloon dilation and usual care, in GBP per person)[33]:

- Initial procedure: additional £1,174 (EAC's estimate) or £742 (company's estimate)
- Adverse events (included in the procedure costs): cost savings of about £48 per procedure
- Repeat procedure – endoscopic management: cost savings of £154 (EAC) or £355 (company)
- Repeat procedure – surgical management (urethroplasty): cost savings of £2,857 (EAC) or £2,856 (company)

- Paclitaxel-coated balloon dilation-related training: an additional £3 (EAC) or £9 (company)
- Asymptomatic health state: an additional £65 (EAC and company)
- Symptomatic health state: cost savings of £107 (EAC and company)

Sensitivity Analysis Results

Almost all sensitivity analyses done by the EAC and the company showed robust results in terms of cost savings with paclitaxel-coated balloon dilation[33] as follows (savings shown as negative values):

- In deterministic sensitivity analyses, savings were shown for natural history, effectiveness, and cost inputs, for example:
  - Starting age (base case, 59 years): 43 and 75 years; −£2,518 and −£2,428 per patient, respectively
  - Monthly probability of symptom recurrence with paclitaxel-coated balloon dilation (base case, 2.6%): 0.5% and 3.3%; −£5,194 and −£1,918 per patient, respectively
  - Monthly probability of symptom recurrence with urethroplasty (base case, 0.9%): 0.7% and 1.2%; −£2,233 and −£2,760 per patient, respectively
  - Probability of getting treatment after recurrence (base case, 90%): 67.5% and 100%; −£2,465 and −£2,501 per patient, respectively
  - Probability of getting treatment after recurrence (base case, 70%): 52.5% and 87.5%; −£3,141 and −£1,995 per patient, respectively
  - Treatment cost (urethroplasty) (base case, £4,761.47): £3,571 and £6,139; −£1,790 and −£3,325 per patient, respectively
  - Total treatment cost including the device (Optilume; base case, £1,986): £1,554 and £2,418; −£3,135 and −£1,869 per patient, respectively
  - Cost of device (Optilume; base case, £1,350): £1,012.50 and £1,687.50; −£2,996 and −£2,007 per patient, respectively
- Paclitaxel-coated balloon dilation was cost-saving in scenarios addressing:
  - Urethroplasty as the main comparator to paclitaxel-coated balloon dilation, −£243 per person
  - Changes in the baseline discount rate (3.5%), 2% and 4%; −£1,391 and −£3,175 per patient, respectively
  - Duration of the time horizon, 1 and 20 years; −£1,391 and −£3,175 per patient, respectively (at the base case of the device of £1,350)
  - Setting for the paclitaxel-coated balloon dilation procedure, 50% and 50% for day case vs. outpatient setting (this was a setting assumption of the original company's analysis)
- Probabilistic analysis found paclitaxel-coated balloon dilation was cost saving 86% of the time assuming that it is a day-case procedure in 100% of cases (EAC analysis)[33]

The key driver that was found to cause a switch from cost savings to cost increases with paclitaxel-coated balloon dilation was the probability of recurrence with the usual care procedures, and the effectiveness of paclitaxel-coated balloon dilation for repeated interventions[33]:

- In one-way deterministic analysis, when the monthly probability of recurrence with the usual care procedures was smaller than with paclitaxel-coated balloon dilation (1.9% vs. 2.6%), meaning that usual care was more effective than paclitaxel-coated balloon dilation, there were additional costs of £1,694 per procedure
- A two-way deterministic analysis showed that paclitaxel-coated balloon dilation was not cost saving when there was a high chance of the recurrence with both the usual care (> 17% per month vs. 16.3% in the base case) and the paclitaxel-coated balloon dilation (> 9% vs. 2.6% in the base case) procedures, and when the absolute difference in the probability of the stricture recurrence between these 2 options (i.e., effectiveness) was less than 10% (vs. > 13% in the base case). These analyses suggested remaining uncertainty related to the repeated use of paclitaxel-coated balloon dilation following an initially failed procedure

In summary, based on these cost-consequence analyses, paclitaxel-coated balloon dilation was cost saving compared with the usual care represented by a mix of urethral dilation and DVIU procedures. Clinical experts in the UK considered this comparator appropriate for their health care system for 2 reasons[33]:

- A mix of endoscopic procedures was used for retreatment of male bulbar urethral strictures in the UK practice
- All standard care endoscopic procedures were equally non-effective for treating recurrent urethral strictures (i.e., no statistically significant differences between them in the efficacy for prevention of recurrent strictures over time)

Although these analyses did not establish the cost–utility of paclitaxel-coated balloon dilation, experts[33] who reviewed the report agreed that the treatment with paclitaxel-coated balloon dilation was effective, minimally invasive, associated with minimal side effects, and had a potential to reduce the need for retreatments and invasive surgical procedures.[33] They agreed that it could be considered an alternative to standard endoscopic management and would delay the need for urethroplasty.

Table 8: Characteristics of Studies Included in the Economic Literature Review

	Analysis: methods				Results			
Author, year, country, intervention, comparator	**Technique/model**	**Perspective**	**Time horizon (discount rate)**	**Population**	**Health outcomes**	**Costs (GBP)[a]**	**Mean difference: I vs. C**	**Cost-effectiveness: reference case and sensitivty analysis**
NICE (MTG73), 2022,[33] UK	Cost–consequence analysis/ Markov (state-transition) model, monthly cycle	Single-payer (NHS and PSS)	5 y (3.5%)	Adult men with recurrent bulbar urethral strictures ≤ 3 cm and failed ≥ 1 prior endoscopic procedure (DVIU or dilation) Mean age: 59 y (range: 44–74 y)	No. of total repeat procedures per 100 over 5 y	Mean over 5 y: 2019/20; Optilume device cost: £1,350		Optilume was cost saving compared with endoscopic management or urethroplasty in the base case and scenario analyses, addressing the setting and time horizon; in most one-way sensitivty analyses addressing parameter model uncertainty, Optilume remained cost-saving In probabilistic analysis for the base case parameters, Optilume was cost saving 86.0% of the time compared with endoscopic management
I: Optilume	—	—	—	—	Y1, 19.9 Y5, 111	Annual: NR Total, 5 y (company): £6,620 Total, 5 y (NICE-EAC): £7,249[b]	Mean difference, repeat procedures per 100 at 5 y: 120.3 (1.2 per person)	Key driver from deterministic one- and two-way analyses was baseline recurrent rate with endoscopic management and effectiveness of Optilume for the next, repeated procedure
C (base case): standard care with endoscopic management procedures (combination of urethral dilatation [S-curve dilators or rigid rod {metal or plastic} dilation] and DVIU)	—	—	—	—	Y1, 85.4 Y5, 231.2	Annual: NR Total, 5 y (company): £9,122 Total, 5Y (NICE-EAC): £9,126	Mean difference in costs at 5 y (company): −£2,502 Mean difference in costs at 5 y (EAC): −£1,877	
C (scenario): urethroplasty (surgery)	—	—	—	—	NR	Annual: NR Total, 5 y (company): £6,863	Mean difference in costs at 5 y (company):−£243	
Kelly, 2023[34] UK	Cost–consequence analysis/ Markov (state-	Single payer (NHS and PSS)	5 y (3.5%)	Adult men with recurrent bulbar	No. of total repeat procedures per 100 over 5 y	Mean over 5 y: 2019/20; Optilume device cost: £1,350		Optilume was cost saving compared with endoscopic management or urethroplasty in the base case and scenario

Author, year, country, intervention, comparator	Analysis: methods				Results			
	Technique/model	Perspective	Time horizon (discount rate)	Population	Health outcomes	Costs (GBP)[a]	Mean difference: I vs. C	Cost-effectiveness: reference case and sensitivty analysis
Note: same analysis and results done by company (initially submitted to NICE)	transition) model, monthly cycle			urethral strictures ≤ 3 cm Mean age: 59 y (range: 44–74 y)				analyses, addressing the setting and time horizon; in most one-way sensitivty analyses addressing parameter model uncertainty, Optilume remained cost-saving In probabilistic analysis for the base case parameters, Optilume was cost saving 94.3% of the time compared with endoscopic management
I: Optilume	—	—	—	—	Y1, 19.9 Y5, 111	Annual: NR Total, 5 y (company): £6,620[b]	Mean difference, repeat procedures per 100 at 5 y: 120.3 (1.2 per person)	Key driver from deterministic one- and two-way analyses was baseline recurrent rate with endoscopic management and effectiveness of Optilume for the next, repeated procedure
C (base case): standard care with endoscopic management procedures (combination of urethral dilatation [S-curve dilators or rigid rod {metal or plastic} dilation] and DVIU)	—	—	—	—	Y1, 85.4 Y5, 231.2	Annual: NR Total, 5 y (company): £9,122	Mean difference in costs at 5 y (company): −£2,502	
C (scenario): urethroplasty (surgery)	—	—	—	—	NR	Annual: NR Total, 5 y (company): £6,863	Mean difference in costs at 5 y (company): −£243	

Abbreviations: C, comparator; DVIU, direct visual internal urethrotomy; GBP, Great British Pound; I, intervention; NHS and PSS, National Health Service and Personal Social Services; NICE, National Institute for Health and Care Excellence; NR, not reported; Y, year

[a]Minus signs indicate savings.

[b]The company's (Laborie Medical Technologies) model assumption for the setting of treatment with Optilume: hospital day case setting 50%, 50% outpatient; EAC's de-novo assumption: day case setting 100%. Hence, results presented for both analyses.

Applicability and Limitations of the Included Studies

Appendix 3 provides the results of the quality appraisal checklist. Overall, the included studies were deemed partially applicable to the research question and Ontario context (Table A9). Even though the applicability of the study population and intervention was fully appropriate, it was only partially applicable for other important factors, for instance:

- Differences between the UK and Ontario in the clinical treatment pathway – namely, the second use of paclitaxel-coated balloon dilation following urethral stricture recurrence may not be appropriate for Ontario because of the lack of efficacy data and uncertainty in the successfulness of the treatment with multiple use of paclitaxel-coated balloon dilation over time compared with urethroplasty. In this case, urethroplasty, rather than reuse of paclitaxel-coated balloon dilation, would be recommended (S. Neu, MD, oral and email communications, December 13, 2024; R. Matta, MD, oral and email communications, March 10, 2025). These differences in the clinical treatment pathway, including the paclitaxel-coated balloon procedure, would impact the economic model structure following a treatment failure
- Differences between the UK and Ontario health care systems may yield different costs of urethral stricture procedures even though paclitaxel-coated balloon dilation resulted in cost savings when extremely high procedure costs were assumed in one-way deterministic sensitivity analysis[33]
- Differences in the reference case discount rate between NICE and Canada's Drug Agency (CDA) (3.5% vs. 1.5%), though no switch in the reference case results from savings to additional costs, were found when 2% and 4% discount rates were assumed in one-way sensitivity analyses[33]

As shown in Table A10, we deemed other methodological limitations of the NICE assessment and a study by Kelly et al (i.e., same data presented in the 2022 NICE MTG73 report)[33,34] as potentially serious and not very serious, for the following reasons:

- *Assessment of QALYs.* There is no comparative effectiveness assessment of paclitaxel-coated balloon dilation versus usual care treatment over a long-time horizon, and no measurement of changes in QALYs over time with recurrent urethral strictures; hence, no cost–utility analysis was used to address the value for money. Instead, the company and EAC resorted to cost–consequence analyses to examine the value of paclitaxel-coated balloon dilation, which further supported a conditional recommendation for the use of paclitaxel-coated balloon dilation. The authors included a request for submission of long-term RCT data when they become available for a re-assessment
- *Uncertainty in the main model inputs.* Paclitaxel-coated balloon dilation was cost-saving regardless of duration of the time horizon at a base case device price of £1,350 (2019/20)[33]; we considered this use of short time horizons more appropriate because of the short duration of currently available comparative studies and the very limited comparative evidence on the effectiveness of urethroplasty versus paclitaxel-coated balloon dilation for recurrent urethral strictures. Also, overly optimistic extrapolation of the recurrence of urethral strictures over a period of 20 years or lifetime may not be reliable given the lack of published long-term comparative data. In addition, the price of

the device is uncertain – it may increase over time or may be different for Canada compared with the UK. A substantial increase in the device price could result in additional costs rather than savings over a short-term time horizon

Discussion

Our review identified 2 UK-based cost–consequence studies[33,34] comparing paclitaxel-coated balloon dilation with usual endoscopic management (a mix of various types of urethral dilation procedures and DVIU) for male bulbar urethral strictures in adults.[33,34] Both studies concluded that, compared with usual care, paclitaxel-coated balloon dilation would reduce the need for retreatment (1.20 fewer repeated procedures per person over 5 years) and reduce costs (by £1,877 per person at 5 years).[33] When compared with urethroplasty, the savings were smaller (£243 per person). These findings remained robust across most sensitivity analyses, including longer time horizons and changes in the discount rate or device cost (upper bound of £1,687.50, corresponding to $3,545 CAD in 2024).

Key factors found to influence the economic study results were the probability of recurrence with the usual care procedures and the long-term effectiveness of repeated paclitaxel-coated balloon dilation for subsequent recurrent bulbar urethral strictures. This finding suggested a gap in the evidence – specifically, the lack of long-term RCT data to confirm the extent and duration of its benefit for recurrent bulbar urethral strictures.

While these studies offer valuable insights, they are not directly applicable to the Ontario context due to potential differences in health care systems, procedure costs, and clinical treatment pathways between the UK and Ontario – all of which could affect the model structure and results. Although the authors of the ROBUST III RCT reported changes (improvements) in disease-specific quality of life (assessed by a single question of the IPSS[33]), no changes in health-related quality of life were measured by any recommended instrument (e.g., EQ-5D), making it difficult to reliably estimate the benefit of paclitaxel-coated balloon dilation in QALYs. While NICE-MTAC[33] used the findings of the model-based cost–consequence analyses to provide a conditional recommendation for the use of paclitaxel-coated balloon dilation for treatment of recurrent bulbar urethral strictures in males, they are awaiting results of a long-term 5-year ROBUST III RCT (NCT03499964) that may enable a more thorough effectiveness assessment.

Equity Considerations

None of the included economic studies evaluated differences in the access and costs of paclitaxel-coated balloon dilation or other usual care endoscopic procedures between vulnerable, trans-identifying, or Indigenous male populations and the general population. Paclitaxel-coated balloon dilation may be a costly procedure and only some people could afford to pay it out of pocket. Therefore, income, social status, and ethnicity could increase a person's vulnerability and may contribute to inequities in access to care in Ontario, leading to suboptimal health outcomes in some population subgroups. In addition, as pointed out in the clinical evidence review, a potential equity issue specifically related to paclitaxel-coated balloon dilation is the possibility of paclitaxel affecting semen quality, testicular function, and fertility. These issues are to be examined in an on-going post market study (Optilume post-approval clinical evaluation of andrology parameters, STREAM: NCT05383274).

Strengths and Limitations

We comprehensively reviewed the economic literature by systematic searches of electronic databases, grey literature sources, and reference lists. It is unlikely that we overlooked any relevant study. However, we identified only 2 relevant costing studies in adults and no studies in youth, probably because of the small prevalence of urethral strictures in young males. The included studies considered the UK public-payer perspective; if they were to use the societal perspective and account for indirect (productivity loss) and non-medical direct costs, then cost-savings with paclitaxel-coated balloon dilation could be larger.

Limitations of our review are related to the limitations of the current clinical evidence, which lacks long-term effectiveness data for paclitaxel-coated balloon dilation to support long-term cost-effectiveness modeling of its use for recurring urethral strictures.

Conclusions

Based on our review of the 2 economic studies from the UK,[33,34] urethral dilation with the paclitaxel-coated balloon catheter is potentially cost saving at 5 years compared with usual endoscopic procedures (urethral dilatations and DVIU) for the treatment of recurrent and symptomatic bulbar urethral strictures of 3 cm or less in adult males. However, these studies were associated with methodological limitations and were not directly applicable to the Ontario context. Thus, the cost-effectiveness of publicly funding paclitaxel-coated balloon dilation for recurrent bulbar urethral strictures in adult males in Ontario is unknown.

Primary Economic Evaluation

Our economic literature review did not identify any cost-effectiveness studies comparing urethral dilation with a paclitaxel-coated balloon catheter with usual care procedures (i.e., endoscopic management that includes 1 or more types of urethral dilation procedures, including direct vision internal urethrotomy [DVIU]). As such, we conducted a primary economic evaluation to address our research question below. We identified 2 economic studies[33,34] that have some methodological limitations and are not directly applicable to the Ontario context.

Research Question

What is the cost-effectiveness of urethral dilation with a paclitaxel-coated balloon catheter compared with usual care for the treatment of adult males with recurrent and symptomatic bulbar urethral strictures from the perspective of the Ontario Ministry of Health?

Methods

The information presented in this report follows the reporting standards set out by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[39] The content of this report is based on a previously developed economic project plan.

Type of Analysis

We conducted a model-based cost-effectiveness analysis over a 5-year time horizon. The analysis compared direct health care costs and the probability of recurrence of urethral stricture after the initial procedure (reference case). The probability of urethral stricture recurrence was derived from data on freedom from reintervention that was consistently observed over time. We also compared procedure-related adverse events such as hematuria, dysuria, and urinary track infections (UTIs). However, we did not model the recurrence of urethral strictures from other clinical end-points, such as anatomical success at 6 months or improvement in the International Prostate Symptom Score (IPSS) of at least 30% without repeat intervention, because of the limitations of the published primary study evidence and lack of clearly reported changes over time in these clinical end-points that could have been used to support an extrapolation of the effectiveness of paclitaxel-coated balloon dilation over 5 years.

We did not conduct a cost–utility analysis due to the absence of reliable and valid health utility data. None of the economic studies or clinical trials of paclitaxel-coated balloon dilation in people with recurrent urethral strictures measured or reported changes in health-related quality of life using recommended instruments (e.g., EQ-5D).[40] As a result, it is difficult to estimate the incremental and temporal quality-adjusted life-year (QALY) benefit of paclitaxel-coated balloon dilation. Also, we did not have access to individual-level data from the ROBUST III randomized controlled trial (RCT) needed to apply the published mapping algorithm[41] for converting IPSS scores into EQ-5D utilities for QALY estimation.

Population of Interest

Our population of interest was adult males with recurrent, symptomatic bulbar urethral strictures of 3 cm or more in length, who had been unsuccessfully treated with prior endoscopic procedures. The starting mean age of the cohort was assumed to be 45 years in the reference case, based on the natural and clinical history of the urethral stricture disease, but other values for the age range were tested in a sensitivity analysis (S. Neu, MD, oral and email communications, December 13, 2024, and March 10, 2025).

We did not conduct an equity-related subgroup analysis due to limited data. More research is required to describe how different sub-populations might access paclitaxel-coated balloon dilation in Ontario.

Perspective

We conducted the analysis from the perspective of the Ontario Ministry of Health.

Interventions and Comparators

Table 9 summarizes strategies evaluated in the economic model.

Table 9: Intervention and Comparator Evaluated in the Economic Model

Intervention	Comparator	Population	Outcomes[a]
Urethral dilation with a paclitaxel-coated balloon catheter	Usual care: mix of urethral dilation procedures or DVIU (endoscopic management)	Adult males with recurrent bulbar urethral strictures ≤ 3 cm in length who have been unsuccessfully treated with endoscopic procedures	Recurrence of urethral strictures after the initial prcedure as determined from the clinical outcome: freedom from reintervention Safety outcomes: procedure-related AEs Direct health care costs

Note: Paclitaxel-coated balloon dilation was not considered a first-line treatment option for recurring bulbar strictures, but as an option after unsuccessful treatments with current endoscopic management procedures such as DVIU.

Abbreviations: AE, adverse events; DVIU, direct vision internal urethrotomy.

[a]ICER is estimated from the cost and effectiveness (clinical) outcome.

For these 2 model strategies, we made the following assumptions in alignment with expert inputs (S. Neu, MD, and R. Matta, MD, email and oral communications, December 13, 2024, to August 25, 2025):

- Comparator for treating recurrent bulbar urethral strictures: a mix of endoscopic management procedures including DVIU, rather than solely DVIU
  - This has been a common practice in Ontario (S. Neu, MD, email and oral communications, December 13, 2024, and March 10, 2025)
  - There is no difference in the effectiveness between various endoscopic procedures, including DVIU, on the recurrence of urethral strictures in adult males[15,33]
- Intervention: appropriate use of the paclitaxel-coated balloon catheter

- Not a first-line treatment for recurrent bulbar strictures[33]
- An alternative to recurrent endoscopic procedures and urethroplasty (S Neu, MD, and R. Matta, MD, email and oral expert communications, March 9–10, 2025)
- One-time use only in eligible people after they are unsuccessfully treated with various endoscopic procedures, including DVIU (S Neu, MD, email and oral communications, December 13, 2024, and March 10,2025)

In addition, based on our expert consultations, we included other model strategies in our scenarios:

- Urethroplasty as a separate alternative to be compared with paclitaxel-coated balloon dilation (R. Matta, MD, email and oral communications, March 9–10,2025). Of note, the usual care or intervention strategy considered urethroplasty in the reference case treatment pathway following an unsuccessful endoscopic procedure treatment
- Paclitaxel-coated balloon dilation following urethroplasty as a possible intervention (because it may be used off-label in the common clinical practice; S Neu, MD, email and oral communications, December 13, 2024, and March 10, 2025)

Treatment Pathways

Figure 4 was used to conceptualize the economic model. It presents simplified treatment pathways for the intervention or usual care strategies (S. Neu, MD, and R. Matta, MD, oral and email communications, December 13–16, 2024, March 10 and August 25, 2025):

- Prior workups for establishing the diagnosis of recurrence were considered to be similar between strategies, with the exception of the use of a retrograde urethrogram with or without a voiding cystourethrogram before the paclitaxel-coated balloon dilation procedure. This strategy was included only in the costing of the intervention
- A person with a diagnosed recurrent bulbar urethral stricture who was previously treated with endoscopic management procedures would be treated again with urethral dilation endoscopic procedures in the usual care strategy or with paclitaxel-coated balloon dilation in the intervention strategy
- Paclitaxel-coated balloon dilation would be used only once in a patient's lifetime
- The next procedure offered after an unsuccessful endoscopic or paclitaxel-coated balloon dilation procedure would be urethroplasty (the probability of accepting surgical treatment was included in the model)
- Repetitive use of urethroplasty was not considered in the reference case because the treatment pathways were not modeled beyond a 5-year time horizon
- People who could not accept surgical treatment with urethroplasty would be conservatively treated (management of the symptoms), with regularly scheduled urologist follow-ups, including:

  - Urethral dilation (ambulatory, in endoscopic suites) done regularly (e.g., every 6–12 months); we made a simplifying modeling assumption to have it done once per year, or
  - Use of self-catheterization or indwelling catheters instead of recurring dilation procedures, even though neither of these 2 catheterization options is currently reimbursed by the Ministry of Health (Ministry of Health Research Analysis and Evaluation Branch, oral and email communication, April 2025)
- For recurring urethral strictures after unsuccessful treatment with urethroplasty, we assumed the same follow-up options as those mentioned above (Figure 4)

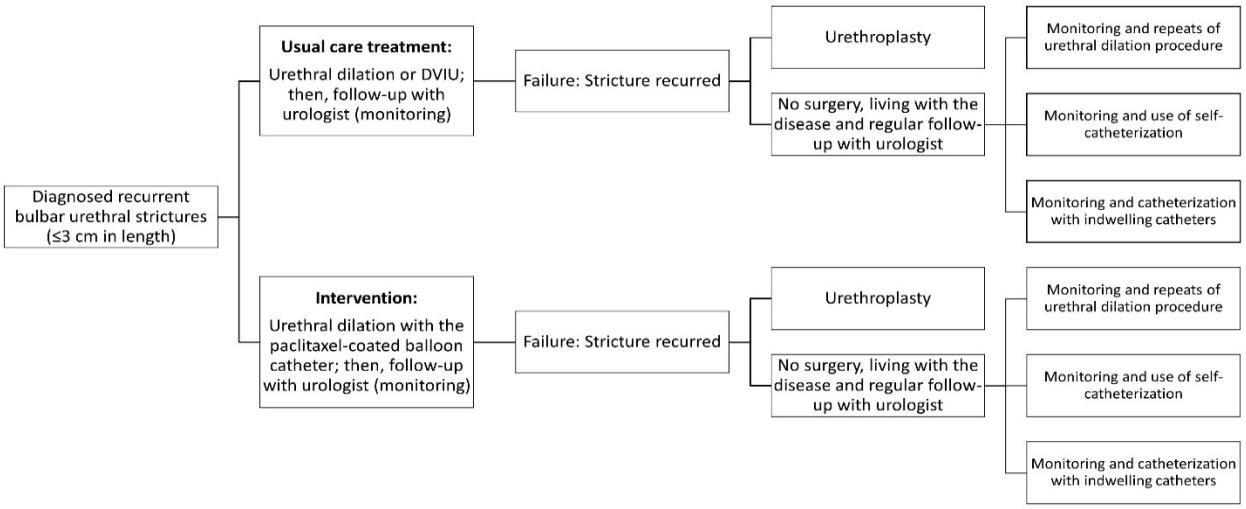

Figure 4: Simplified Treatment Pathways, Usual Care and Intervention

This schematic summarizes simplified treatment pathways for adult males with diagnosed recurrent bulbar urethral strictures ≤ 3 cm in length, which was further used to inform the decision-model structure. In the usual care pathway, after an unsuccessful endoscopic procedure there is a possibility to undergo a urethroplasty or to forgo this invasive surgical option and continue to be followed up by urologists with the following 3 options: (1) monitoring and repeats of urethral dilation procedures, (2) monitoring and use of self-catheterization, or (3) monitoring and catheterization with indwelling catheters. In the intervention pathway scenario, paclitaxel-coated balloon dilation could be used only once during a patient's lifetime (S. Neu, MD, oral and email communication, December 13, 2024, and March 10, 2025). Thus, if the stricture reoccurs after the paclitaxel-coated balloon intervention, surgery with urethroplasty or non-surgical follow-up options described above would be offered.

Note: This novel procedure was not considered a first-line treatment option for recurring bulbar strictures but as an option after unsuccessful treatments with current endoscopic management procedures such as DVIU.

Abbreviations: DVIU, direct vision internal urethrotomy.

Time Horizon and Discounting

We used a 5-year time horizon for our reference case analysis and applied an annual discount rate of 1.5% to both costs and health outcomes incurred after the first year.[40] We did not explore a lifetime horizon because the ROBUST III RCT reported only up to 3-year effectiveness data for paclitaxel-coated balloon dilation.[26] Moreover, ROBUST III was a cross-over trial – while it provided comparative estimates for year 1, data for years 2 and 3 were reported only for the paclitaxel-coated balloon dilation arm. The

methodological quality of this evidence was assessed as low (GRADE: Low and Very low, see clinical evidence review).

Main Assumptions

The model's main assumptions, established in consultation with experts (S. Neu, MD, email and oral communications, December 13, 2024, and March 10, 2025; R. Matta, MD, email and oral communications March 9–10 and August 25, 2025) are described here (we report other simplifying assumptions on the model structure and inputs in the next sections):

- A mix of usual care endoscopic procedures currently used for treating recurrent urethral strictures in Ontario (i.e., various types of urethral dilation procedures and DVIU) represents a reasonable and appropriate comparator for this analysis (S. Neu, MD, email communication, December 13, 2024)
- The effectiveness of all usual care endoscopic procedures over 1 year is similar[15,33]
- Urethral dilation with paclitaxel-coated balloon dilation could be used only once in the clinical pathway for the treatment of recurrent bulbar urethral strictures (≤ 3 cm in length) in a patient's lifetime (S. Neu, MD, email communication, December 13, 2024)
- Paclitaxel-coated balloon dilation is provided in hospital day surgery settings (including ambulatory endoscopy suites) because it requires sedation and local anesthesia (S. Neu, MD, email and oral communications, December 13, 2024, and March 10, 2025; R. Matta, MD, oral communications, August 25, 2025)
- Paclitaxel-coated balloon dilation could be considered as an alternative to current endoscopic procedures, not as a first-line treatment; more likely among the last non-invasive options considered for bulbar urethral stricture treatment before urethroplasty
- Effectiveness of paclitaxel-coated balloon dilation on all anterior and bulbar urethral strictures is similar (reference case, tested in sensitivity analysis)
- People who are offered paclitaxel-coated balloon dilation would accept it (reference case, tested in sensitivity analysis)

Model Structure

We developed a probabilistic Markov (state-transition) cohort model that was informed by the treatment pathway in Ontario presented in Figure 4 and also by previously published economic models[33,34] assessed in our evidence review. The Markov model simulated the cohort's outcomes over 5 years, using a cycle length of 1 month (half-cycle correction applied). Figure 5 shows a simplified model structure, while clinical and cost model input parameters used to populate the model are presented in the next sections.

The reference case model simulation for both strategies started with a short (temporary) Markov health state:

- "Endoscopic procedure" considers only 1 cycle or the first month of model simulation, during which period members of the patient cohort would have their usual care or paclitaxel-coated balloon procedure. In this health state, we accounted for:

  - Patient participation in the endoscopic procedures
  - Diagnosis of the recurrent bulbar urethral stricture ≤ 3 cm in length, including additional diagnostic test costs associated with paclitaxel-coated balloon dilation only (e.g., a retrograde urethrogram with a voiding cystourethrogram)
  - Procedure-related costs
  - Chance of procedure-related adverse events and their costs
- Following the procedure state, all cohort members were assumed to be successfully treated and would transition to another Markov health state – "living without symptoms of the urethral stricture (asymptomatic) after endoscopic procedure" – in which they could reside and be monitored on a monthly basis for the rest of the time horizon, or in the case of the stricture recurrence, they would transition into another Markov health state – "living with the urethral stricture (symptomatic) after endoscopic procedure." The probability of stricture recurrence was informed by data from the ROBUST III RCT (primary outcome for the reference case: freedom from the reintervention),[24,26,33] and other published long-term evidence[42]
- From the latter state (also described above and in Figure 4), we modeled a surgical or several non-surgical treatment follow-up options for the management of recurring urethral strictures. These options were included as separate, additional health states (Figure 5) as follows:
  - Some cohort members would decide to undergo urethroplasty and transition into the second temporary Markov state – "urethroplasty" – which served to accumulate the costs of the procedure and potential procedure-related adverse events over 1 month before the cohort's next transition. Similar to the prior analyses,[33,34] we adjusted the probability of transitioning to this state for currently published waiting times for the urological procedures in Ontario (average: 120–130 days[43]) and acceptance of the urethroplasty treatment (i.e., 90% participation in the reference case)
  - Following urethroplasty, the cohort would transition and reside in an asymptomatic Markov health state*:* "living without symptoms of the urethral stricture after urethroplasty." Some of this cohort could suffer a recurrence of the urethral stricture and transition to another Markov health state "living with the urethral stricture after urethroplasty." Like the prior analyses, the stricture recurrence after urethroplasty was informed by the probabilities of the OPEN clinical trial.[37,38]
  - Cohort members who decided not to undergo urethroplasty or who failed urethroplasty would continue to live with recurring urethral strictures in 1 of the 3 Markov health states that account for urologist care until the end of simulation or death (whichever occurs first):
    - A health state of regular specialist follow-up (e.g., every 6–12 months), including a possibility of continuing ambulatory-performed urethral dilations
    - A health state of regular specialist follow-up with the patient choosing self-catheterization to manage symptoms of the recurrent urethral stricture disease

- A health state of regular specialist follow-up with the patient choosing indwelling catheters to manage symptoms of the recurrent urethral stricture disease

- All of these states considered the costs of health care professional services, procedures, and costs of procedure-related adverse effects (described in the next section). Costs of an intermittent catheter used for self-catheterization and costs of an indwelling catheter were not included in the reference case because they are not covered by the Ministry, but they were included in a separate scenario addressing additional out-of-pocket direct medical costs paid by the patient

From any of the above-mentioned health states, people would have a chance of dying and would then transition into the absorbing death state. We did not model procedure-specific mortality due to a lack of evidence but assumed that this risk was amortized in the overall background mortality.

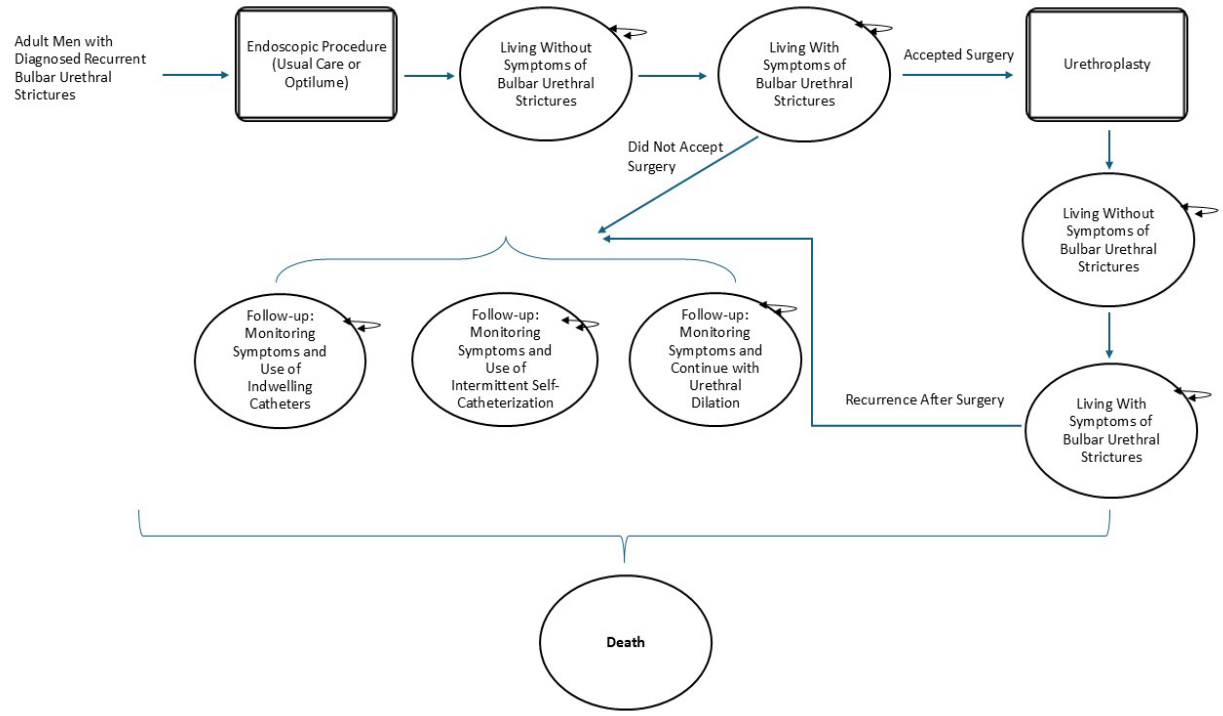

Figure 5: Simplified Markov Model Structure Used for Reference Case

We developed a probabilistic Markov (state transition) model for adult males diagnosed with a recurrent bulbar urethral stricture ≤ 3 cm in length, eligible for treatment with the usual care or paclitaxel-coated balloon dilation procedures. This novel procedure was not considered a first-line treatment option for recurring bulbar strictures, but as an option after unsuccessful treatments with current endoscopic management procedures such as DVIU.

Clinical Outcomes

We obtained the clinical parameter values for usual care and intervention treatment pathways from the published studies identified in our clinical evidence and economic evidence reviews.

Natural and Clinical History

Table 10 presents main inputs that informed economic modeling of the usual care pathway (Figure 4):

- Effectiveness and safety of the usual care procedures were based on data from the ROBUST III RCT, which compared paclitaxel-coated balloon dilation with endoscopic management (mix of urethral dilation and DVIU) in adult males with recurrent anterior urethral strictures (of which 92.1% were bulbar site strictures) as follows[24-26]:
  - We used freedom from reintervention (retreatment) to define the effectiveness of the usual care procedures on urethral stricture recurrence over time. For this outcome, the certainty in the quality of evidence was low (GRADE: Low), mainly due to high risk of bias (e.g., unblinding of patients, measurement bias, and cross-over during the randomization period of 6 months, see clinical evidence review)
  - The safety of usual care endoscopic procedures was also assessed based on the reported data in the ROBUST III RCT (GRADE: Moderate; risk of bias: low) and informed the procedure-related adverse events
  - The probabilities estimated from the published data were transformed into monthly probabilities using the standard calculation procedures[44-46] to inform transitioning of the cohort over time through various health states on a monthly (cycle) basis
- Effectiveness and safety of urethroplasty was informed by short-term recurrence data reported in the OPEN RCT, which is an open-label clinical trial that compared urethroplasty with DVIU in men with recurrent urethral strictures.[37,38] The long-term effectiveness was informed by 10-year survival data (i.e., freedom from reintervention) reported by the TriNetX registry[47]
- Participation in the treatment procedures was assumed (S. Neu, MD, email and oral communications, December 13, 2024, and March 10–30, 2025):
  - For the endoscopic procedures (initial state), we assumed a 100% acceptance rate in the reference case. We tested this value in the sensitivity analysis
  - For urethroplasty, we assumed a 90% acceptance rate in the reference case (and tested a 75% acceptance rate and other values in the sensitivity analysis). We also accounted for a waiting time of 130 days (range: 30–230 days) for urethroplasty, based on reported data (mean days for urologic surgery [priority level 2–4] in the province: 120–130 days, 90th percentile for urologic surgical procedures in Ontario[43]); we tested much longer and much shorter wait times in the sensitivity analyses. These 2 parameters – acceptance rate of the surgery and waiting time – were combined to calculate the probability of having a urethroplasty after the urethral stricture recurrence (see Table 10)

- Use of self-catheterization with intermittent or indwelling catheters and main adverse events associated with their use were informed by the published literature, including a prior Ontario Health HTA (inputs related to the use of daily self-catheterization with a single use noncoated intermittent catheter)[48] and other research[49,50]
- Background mortality, accounted via monthly chance of dying over 5 years in the reference case, was based on the background Ontario mortality estimates for men aged 45 years or older, as provided in the Statistics Canada Life Tables[51]

Table 10: Natural and Clinical History Inputs Used in the Reference Case Model

Model parameters	Mean (95% CI)[a,b,c]	Distribution	Sources
Probability of accepting the treatment of recurrent bulbar strictures with usual care endoscopic procedures	1.00	NA	Model assumption, tested in sensitivity analysis
Effectiveness of paclitaxel-coated balloon dilation versus usual care procedures on recurrence, as defined by the reported percentage of participants with the event freedom of reintervention	–	–	Clinical review and Elliott et al, 2022[24]: ROBUST III, all strictures regardless of their location
• At 12 mo, usual care, not retreated	21.7%	NA	Clinical review and Elliott et al, 2022[24]: ROBUST III (published data, based on KM curve, Figure 3)
○ Probability, usual care, no recurrence, per month	0.02[a]	Beta[a]	Estimated, constant input probability used over 60 mo and parametrized via the use of hazard table distribution
○ Probability, usual care, no recurrence, extrapolated over 24 mo	0.06167		
Main procedure-related adverse events with usual care endoscopic procedures	–	–	Elliot et al, 2022[24] (ROBUST III data)
• Haematuria, mild	1/48 (2.1%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
• Dysuria, mild	1/48 (2.1%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
• UTI, total	5/48 (10%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
○ UTI, serious	0/48 (0%)	NA	EunetHTA, 2023[52] (ROBUST III data)
• Urinary retention, total	4/48 (8%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
○ Urinary retention with readmission	3/48 (6.3%)	NA	EunetHTA, 2023[52] (ROBUST III data); modeled as conditional: 3/4 (0.75)
• Erectile dysfunction, mild	1/48 (2.1%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
Probability of accepting urethroplasty as the next treatment	0.90	Fixed	Exert communication: S. Neu, MD, December 13, 2024; tested in sensitivity analysis: 0.75

Model parameters	Mean (95% CI)[a,b,c]	Distribution	Sources
Waiting time for urethroplasty	130 d (30–230 d)	Triangular	Estimated based on OH Surgery Dashboard: 90p wait time for urologic surgery; tested in sensitivity analyses to account for longer wait time, of up to 2/3 years)[43]
Probability of retreatment with urethroplasty (after accounting for the waiting time and probability of acceptance), per month[d]	0.318	–	Estimated
Effectiveness of urethroplasty vs. DVIU on the recurrence of urethral stricture, 0–24 mo	–	–	Pickard et al, 2020[38] and Goulao et al, 2020[37]; OPEN RCT
• At 24 mo, urethroplasty, recurrence	20.4%	NA	OPEN RCT: at 2 years, 19 of 93 patients recurred[37,38]
○ Per month probability, urethroplasty recurrence over 0–24 mo	0.009461	Hazard Table Distribution	Estimated: constant input probability parametrized from 0 to 24 mo and estimated hazard table distribution
Effectiveness of urethroplasty (anterior) vs. endoscopic management, survival (event: no reintervetion) at 10 y	72.2%	–	Prebay et al, 2023[47]
• Per month probability, urethroplasty, no retreatment, 24–60 mo	0.00145	Hazard Table Distribution	Estimated: constant input probability of no reintervetion parametrized from 24 to 60 mo using the estimated hazard table distribution
Main procedure-related adverse events following urethroplasty	–	–	OPEN RCT[37,38]
• Haematuria	2%[a]	Beta	Pickard et al, 2020[38] OPEN HTA, Table 20
• UTI	3.1%[a]	Beta	Pickard et al, 2020[38] OPEN HTA, Table 20
• Wound infection	1%[a]	Beta	Pickard et al, 2020[38] OPEN HTA, Table 20
• Readmission to hospital	3.1%[a]	Beta	Pickard et al, 2020[38] OPEN HTA, Table 20
• Erectile dysfunction	5%[a]	Beta	Pickard et al, 2020[38] OPEN HTA, Table 19
Probability of not having surgical procedure, monthly	1–0.318[d]	–	Estimated from the data above[d]
For those who did not have the urethroplasty, follow-up with either			
• Dilation (procedure)	80%	Dirichlet	Estimate: assumed to be the highest of the 3 options as it is publicly funded (the spread was tested in sensitivty analysis)
• Indwelling catheter	5%		Campeau et al, 2020
• ISD	15%		Estimated: 100%–80%–5%

Model parameters	Mean (95% CI)[a,b,c]	Distribution	Sources
Probability of main adverse events due to self-catheterization or indwelling catheterzation, monthly	–	–	OH-HQO, 2019[48]
• Haematuria (ISD)	0.004396[a]	Beta	OH-HQO, 2019[48]
• UTI (ISD)	0.194802[a]	Beta	Woodbury et al, 2008,[53] OH-HQO, 2019[48]
• UTI (indwelling catheter)	0.40 (SE: 0.001249)[a]		Hird et al, 2021[50]
• Catheter-associated bacteremia and admission to hospital (ISD and indwelling)	0.036 (0.034–0.038)[a]	Beta	OH-HQO, 2019,[48] Bermingham et al, 2013[54]
• Death due to catheter-associated bacteremia	0.00665 (0.00245–0.01761)[a]	Beta	OH-HQO, 2019,[48] Bermingham et al, 2013[54]
Annual probability of all-cause mortality for adult men, starting at the age of 45	0.00244	Age-speciifc Life Table	Males, Ontario Life Tables 2016–2018, Statistics Canada, 2020[51]
• Estimated probability of death, per month[c]	0.0002036	Age-speciifc Life Table	Estimated

Abbreviations: CI, confidence interval; ISD, intermittent self-dilatation (self-catheterization); NA, not applicable; RCT, randomized controlled trial; SE, standard error; UTI, urinary tract infection.

[a]Standard errors were estimated where data was available. Where data was not available, we assumed 10% around the mean.

[b]Beta distributions were assigned to the probability estimates in probabilistic analysis, where appropriate.

[c]Markov model used a cycle length of 1 month and all rates and probabilities were adjusted appropriately.

[d]Monthly probability calculated as[33]: 1 − (1 – [probability of accepting urethroplasty × probability of using urethroplasty])^(30/days waiting)[33,34] = 1 − (1 – [0.9 × 0.9]^[30/130]) = 0.318.

Effectiveness of Paclitaxel-Coated Balloon Dilation

- Additional information related to the effectiveness and safety of paclitaxel-coated balloon dilation for urethral stricture is shown in Table 11. For the reference case, we used data related to the freedom from reintervention outcome that was reported for all anterior urethral strictures because the effectiveness of the intervention over 5 years was more consistently reported over time for all urethral strictures than for the bulbar urethral strictures alone
- As mentioned above, the quality of evidence for the main effectiveness outcomes, which were based on 1-year data from the ROBUST III RCT and its 2- and 3-year extensions of the paclitaxel-coated balloon dilation arm,[24-26] was rated low (GRADE: Low, risk of bias: high, clinical evidence review)
- We examined the robustness of the reference case estimates in a scenario that considered the effectiveness of paclitaxel-coated balloon dilation on the recurrence of bulbar urethral strictures solely based on the 2-year data of the ROBUST III study[25] and 5-year data of the ROBUST I study[42]

Table 11: Effectiveness and Safety of Paclitaxel-Coated Balloon Dilation, Reference Case Model

Model parameters	Mean (95% CI)[a,b,c]	Distribution[a,b,c]	Sources
Probability of accepting the treatment of recurrent urethral stricture with endoscopic procedures	1.00	NA	Model reference case assumption, tested in sensitvity analysis
Effectiveness of paclitaxel-coated balloon dilation (Optilume) vs. usual care procedures on recurrence, as defined by the reported percentage of participants with the event freedom of reintervention	–	–	Clinical review, Elliott et al, 2022,[24] and Van Dyke et al, 2024,[25] all strictures
• At 12 mo, paclitaxel-coated balloon dilation, not retreated	83.2%	NA	Clinical review and Elliott et al, 2022[24]
○ Per month probability, no recurrence, 0–12 mo	0.01521		Estimated: constant probability, parametrized from 0 to 12 mo and estimated using hazard table distribution
• At 24 mo, paclitaxel-coated balloon dilation, not retreated	78.5% (69.2%–87.9%)	NA	Clinical review and ROBUST III, Van Dyke et al, 2024,[25] 2-y follow-up (see Table 3[25])
○ Per month probability, no recurrence, 12–24 mo	0.00400366		Estimated: constant probability over time, parametrized to adjust the probability from 12 to 24 mo and used hazard table distribution
• At 36 mo, paclitaxel-coated balloon dilation, not retreated	71.9%	NA	Clinical review and ROBUST III, Srikanth et al, 2025,[26] 3-y follow-up
○ Per month probability, no recurrence, 24–36 mo	0.00567		Estimated: constant probability over time, parametrized to adjust the probability from 24 to 36 mo using hazard table distribution
• At 5 y (60 mo), paclitaxel-coated balloon dilation, not retreated	71.7%	NA	DeLong et al, 2025,[42] ROBUST I
○ Per month probability, no recurrence, 36–60 mo	0.0000834	Beta[a]	Estimated: constant probability over time, parametrized to adjust the probability from 36 to 60 mo, and used beta distribution (mean probabilities based on the hazard table distribution: 0–60 mo; SE: 10% of the mean[a])
Main procedure-related adverse events with paclitaxel-coated balloon dilation	–	–	Elliot et al, 2021[24] (ROBUST III)
• Haematuria, mild	3/79 (3.79%) [a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
• Dysuria, mild	7/79 (8.9%) [a]	Beta	EunetHTA, 2023[52] (ROBUST III data)

Model parameters	Mean (95% CI)[a,b,c]	Distribution[a,b,c]	Sources
• UTI, total	9/79 (11.4%)[a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
○ UTI, serious	0/79 (0%)	NA	EunetHTA, 2023[52] (ROBUST III data)
• Urinary retention, total	6/79 (7.6%) [a]	Beta	EunetHTA, 2023[52] (ROBUST III data)
○ Urinary retention, serious (with readmission)	1/79 (1.3%)		EunetHTA, 2023[52] (ROBUST III data), modeled as conditional: 1/6 (0.167)
• Erectile dysfunction, mild	0/79 (0%)	NA	EunetHTA, 2023[52] (ROBUST III data)

Abbreviations: CI, confidence interval; NA, not applicable; SE, standard error; UTI, urinary tract infection.
[a]Standard errors were estimated where data was available. Where data was not available, we assumed 10% around the mean.
[b]Beta distributions were assigned to the probability estimates in probabilistic analysis, where appropriate.
[c]Markov model used a cycle length of 1 month and all rates and probabilities were adjusted appropriately.

Cost Parameters

We estimated health care costs related to resource use and medical services for the treatment of bulbar urethral strictures in adult males with usual care options (endoscopic management) or a new intervention including use of paclitaxel-coated balloon dilation (Tables 12–14). The costs were estimated from available Ontario data, through consultations with experts, and from published literature. All costs were expressed in 2025 CAD and, wherever needed, the Consumer Price Index (CPI) was used to adjust input cost values from previous years.[55]

Presently, there is not a dedicated physician billing code for the paclitaxel-coated balloon dilation procedure, and a combination of Ontario Health Insurance Plan (OHIP) billing codes has been suggested for the physician services claim (S. Neu, MD, and R. Matta, MD, oral and email communication, December 13 to August 25, 2025). In the future, if this procedure becomes publicly funded, the Ministry of Health will need to negotiate with the Ontario Medical Association to establish billing codes for the procedure and physician services.

Costing: Usual Care Treatment Pathways

Following the usual care pathway described in Figure 4, we costed medical services and resources incurred for urethral dilation or DVIU procedures (average cost), urethroplasty, and follow-up care (Table 12). All procedure-related costs were assumed as one-time costs. We used costing assumptions based on available data and expert consultation (S. Neu, MD, and R. Matta, MD, oral and email communication, December 13, 2024, to August 25, 2025), as follows:

- **Pre-endoscopic procedure**: As discussed in Treatment Pathways, above, we costed only the tests in the diagnostic workup that are additional and specific to the use of the paclitaxel-coated balloon catheter; e.g., urethrography (see next section and Table 15) (S. Neu, MD, oral and email communications, December 13 and 16, 2024, and March 10, 2025)

- **Endoscopic management**
  - *Procedure*: We costed an endoscopic procedure (urethral dilation or DVIU) using the IntelliHealth National Ambulatory Care Reporting System (NACRS) database for fiscal year 2022/23 (Ontario).[56] From this database, we selected data pertinent to adult males (aged ≥ 20 years) treated in Day Surgery hospital settings for urethral strictures by combining the procedure codes specific to the treatment of urethral strictures (i.e., main treatment procedure as defined by the CCI codes starting with "1PQ50" and aligned with relevant main diagnosis disease codes – namely, ICD-9/ICD-10 codes for unspecified urethral strictures: 598.x/N359)
    - The total mean cost per procedure included indirect and direct procedure cost components and consumables and was estimated at $1,089.58 per person (see Appendix 4)
  - *Physician services* – endoscopic procedure: We used a combination of OHIP fee codes for the billing of usual care endoscopic procedures (i.e., S532 for DVIU, and Z619 and Z621 for urethral dilation in males, which were also reported in the IntelliHealth OHIP Medical Services database for the 2022/23 fiscal year[56]) and explored the frequency of their use to make our assumptions for the costing of physician (medical) services as follows:
    - Of all reported medical service codes for endoscopic procedures, DVIU was the most commonly used in our population (about 50% of the time, based on the spread of the above-mentioned medical service codes). Thus, we assumed a 50/50 split between the DVIU (code: S532) and urethral dilation procedures (Z619 and Z621). We assumed 35% of urethral dilation procedures done with local anesthesia (Z621)
    - We conservatively costed the use of anesthesiologist services with inclusion of 6 basic and additional time units (depending on the duration of the procedure) for 2 of the 3 considered endoscopic management procedures (Table 12):
      - DVIU (S532: 50% of all procedures) accrued up to 60 minutes (i.e., 4 additional time units; R. Matta, MD, oral and email communication, March 9–10 and August 25, 2025)
      - Urethral dilation procedures with general anesthesia (Z619: 15% of all procedures) accrued up to 30 minutes (i.e., 2 additional time units; R. Matta, MD, oral and email communication, March 9 and August 25, 2025)
      - Urethral dilation with local anesthesia (Z621 and G224: 35% of all procedures) did not include any additional anesthesiologist services because all costs were claimed by the surgeon who performed both sedation and the procedure (R. Matta, MD, oral and email communication, March 9 and August 25, 2025)
    - These assumptions on the spread of the procedure use and associated physician fee costs are uncertain because of variability in the clinical practice and were therefore explored in our sensitivity analysis
  - We accounted for *additional post-procedure costs* related to a removal of the Foley catheter for patients who had DVIUs ($18.74 per person; see Table 12 for details)

  - Based on the above-mentioned assumptions, we estimated the mean cost of procedure-related physician services at about $199 per person and the total procedure mean cost at about $1,307 per person (including post-procedure DVIU)

- **Follow-up monitoring and additional care:** details on the costing are shown in Table 12. In brief, the reference case from the Ministry of Health perspective accounted for the cost of follow-up urologist care (monitoring, including typical diagnostic cystoscopy) for asymptomatic and symptomatic patients annually, differentiating more intense monitoring of the symptomatic patients within the first 2 years ($183 vs. $155 per person per year)
  - In symptomatic patients with recurring strictures, we distinguished the costing of urethral dilation procedures from catheter use as follows:
    - In people who did not undergo or who failed urethroplasty and who accepted urethral dilation procedures as a follow-up option for symptom control (see model inputs in Table 12 and Figures 4 and 5), we costed annual use of simple urethral dilations done ambulatory, in the endoscopy suites (estimated mean procedure cost of about $460 [Appendix 4, Table A11]) plus OHIP fees (codes: Z619 and Z621 [50/50 split])
    - For people who chose self-catheterization or indwelling catheters as a follow-up option for symptom control (i.e., they opted out of the surgical option and chose instead non-surgical FU with self-catheterization), we costed the physician or nurse services and catheter-associated adverse events in the reference case (Ministry of Health perspective) and added the device cost, which patients pay out of pocket in 1 scenario (self-catheterization with single-use noncoated intermittent catheter: about $341 per month; indwelling catheter: about $11 per month)
  - In addition, due to large uncertainty and variability in clinical practice related to the follow-up care in symptomatic patients, we tested the model inputs related to the use of different options and their costs in sensitivity analyses

- **Urethroplasty:** in the reference case, urethroplasty was modeled as a follow-up procedure after the stricture recurrence in the treatment pathway (Figure 4):
  - *Procedure*: We estimated the urethroplasty procedure mean cost at about $9,500 per person based on the acute inpatient data reported in the IntelliHealth Case Costing Initiative Tool for fiscal year 2022/23.[56] The total cost included both direct and indirect costs (and consumables) for a length of stay of about 1.4 days (range: 1–4 days, see Appendix 4 for more details)
  - *Physician services*: We used a combination of 3 OHIP fee codes to estimate the cost of physician fees for one-stage urethroplasty assuming no graft: S535, S579 and Z606 (S. Neu, MD, oral and email communication, December 13 and 16, 2024)
    - The total mean cost including urologist/surgeon and anesthesiologist services was estimated at about $1,402 per person (Table 12)
  - The total mean cost of urethroplasty was estimated at about $10,881 per person

Table 12: Usual Care Treatment Pathway – Costs Used in the Reference Case Model (Per Person)

Cost input values	Unit cost, $	Duration or quantity	Total cost, $: mean, SE[a,b]	Distribution	Reference/source
Diagnostic assessment and initial consultation	NA	NA	–	–	Note: we costed only differentials with the new intervention
Procedure: endoscopic management (one-time cost)					
Endoscopic usual care procedure (urethral dilation or DVIU)	**1,089.58**	**1**	**1,089.58**	**Gamma**	Average, all patients, NACRS, day surgery, 2022/23; see Appendix 4 (Table A11)
DVIU: physician service, urologist/surgeon	166.05	0.5[c]	83.03	Fixed	OHIP fee code for DVIU (SoB): S532, urethrotomy, transurethral (visual); used in 50% of all procedures[c]
DVIU: physician service, anesthesiologist, 6 basic units	15.49	6 × 0.50 [c]	46.47	Fixed	OHIP fee code S532 (SoB), 6 basic units for the complexity of work (E023C)[c]
DVIU: physician service, anesthesiologist, 4 time units	15.49	4 × 0.50 [c]	30.98	Fixed	OHIP fee code S532 (SoB), 4 time units for the time spent on the procedure (approximately 45–60 min)[c]
Urethral dilation: physician service, urologist/surgeon	52.70	0.15[c]	7.91	Fixed	OHIP fee code for urethral dilation, general anesthesia (SoB): Z619; used in 15% of all procedures[c]
Urethral dilation: physician service, anesthesiologist, 6 basic units	15.49	6 × 0.15[c]	13.94	Fixed	OHIP fee code Z619 (SoB), 6 basic units for the complexity of work (E023C)[c]
Urethral dilation: physician service, anesthesiologist, 2 basic units	15.49	2 × 0.15 [c]	4.65	Fixed	OHIP fee code Z619 (SoB), 2 time units for the procedure (approximately 15–30 min; R. Matta, MD, personal communication, March 10 and August 25, 2025)[c]
Urethral dilation, local: physician service, urologist/surgeon	19.20	0.35 [c]	6.72	Fixed	OHIP fee code for urethral dilation with local anesthesia (SoB): Z621; used in 35% of all procedures[c]
Urethral dilation, local: physician service, urologist/surgeon, local anesthesia	15.55	0.35[c]	5.44	Fixed	OHIP fee code for local anesthesia by surgeon (SoB): G224 code (R. Matta, MD, personal communication, March 10 and August 25, 2025), no time units; used in 35% of all procedures[c]
Physician service, total cost			**199.13**	NA	Estimate
Post-Procedure: UC, 50% require Foley					
Physician service, urologist: follow-up with urologist	27.80	0.25	6.95	Fixed	OHIP fee code (SoB): A354, follow-up; assuming 25% of physicians would have this visit in hospital, based on expert responses
Foley catheter and drainage bag inserted after the procedure, consumables	10.53	1	10.53	Gamma	Online distributors: SciSupply.ca (January 23, 2025): catheter: $6.90 and leg bag: $3.63; assumed to be covered by hospital budget
Nurse time, wage per minute	0.67[d]	30[d]	20.00[d]	Gamma	Explanation and source[d]
Post-procedure costs (DVIU solely)	37.48	0.50	**18.74**	NA	Estimate
Total initial costs (procedure, physician, and post-procedure costs)			**1,307.45**	NA	Estimate (calculated as: 1,089.58 + 199.13 + 18.74)
Follow-up/monitoring: asymptomatic patients, physician services, annual cost					
Urologist visit (1 per year)	46.80	1	46.80	Fixed	OHIP fee code (SoB): A353, physician visit, R. Matta, MD, personal communication, March 10 and August 25, 2025)

Cost input values	Unit cost, $	Duration or quantity	Total cost, $: mean, SE[a,b]	Distribution	Reference/source
Urologist, check-up	108.3	1	108.30	Fixed	Combination of OHIP codes for cystoscopy check-up (SoB): G475 + G900 + Z606
Asymptomatic patients: total cost per year (physician services)			155.10	NA	Estimate
Follow-up/monitoring: symptomatic patients, physician services, annual cost					
Urologist visit: first visit (2 per year)	46.80	1	46.80	Fixed	OHIP fee code (SoB): A353, physician visit – the first of 2 done within 1 year (R. Matta, MD, personal communication, March 10 and August 25, 2025)
Urologist, check-up	108.3	1	108.30	Fixed	Combination of OHIP fee codes for cystoscopy check-up (SoB): G475 + G900 + Z606
Urologist visit: second visit	27.80	1	27.80	Fixed	OHIP fee code (SoB): A354, physician visit, the second follow-up visit done within 1 year (R. Matta, MD, personal communication, March 10 and August 25, 2025)
Symptomatic patients: total cost per year: years 1 and 2 (physician services)	–	–	**182.90**	NA	Estimate
Urologist visit: first visit (1 per year)	46.80	1	46.80	Fixed	OHIP fee code (SoB): A353, physician visit – the first of 2 done within 1 year (R. Matta, MD, personal communication, March 10 and August 25, 2025)
Urologist, check-up	108.3	1	108.30	Fixed	Combination of OHIP fee codes for cystoscopy check-up (SoB): G475 + G900 + Z606
Symptomatic patients: Total cost per year, years 3 to 5 (physician services)	–	–	155.10	NA	Estimate
Follow-up care procedures: urethral dilation: annual cost					
Endoscopic usual care procedure: urethral dilation	459.94	1	459.94	Gamma	Average cost, day-surgery procedures, type: endoscopy suite (Appendix 4, Table A11)
Urethral dilation: physician service, urologist/surgeon	52.70	0.50	26.35	Fixed	OHIP fee code for urethral dilation, general anesthesia (SoB): Z619; used in 50% of all procedures (simplifying assumption)
Urethral dilation: physician service, anesthesiologist, 6 basic and 2 time units	15.49	(6+2) × 0.5	61.96	Fixed	OHIP fee code Z619 (SoB): 6 basic units for the complexity of work (E023C) and 2 time units for the time spent on the procedure (approximately 15–30 min)
Urethral dilation, local: physician service, urologist/surgeon	19.20	0.50	9.60	Fixed	OHIP fee code for urethral dilation with local anesthesia (SoB): Z621; used in 50% of all procedures (simplifying assumption)
Urethral dilation, local: physician service, urologist/surgeon, local anesthesia	15.55	0.50	7.78	Fixed	OHIP fee code for local anesthesia by surgeon (SoB): G224 code, no time units; used in 35% of all procedures
Urethral dilation, physician services alone, total cost per year			105.69	NA	Estimate
Urethral dilation: total cost per year	–	–	565.63		Estimate
Follow-up care procedures: self-catheterization, monthly cost					
ISD with a single-use noncoated intermittent catheter, per month	341.21[e]	1.00[e]	0[e]	Gamma	Follow-up care with ISD assumed $0 because it is not covered by MOH, and is

Cost input values	Unit cost, $	Duration or quantity	Total cost, $: mean, SE[a,b]	Distribution	Reference/source
					paid out of pocket; the cost of $341.21 applied in a scenario[e]
Follow-up care procedures: indwelling catheter, monthly cost					
Physician service, urologist: follow-up with urologist	27.80	0.25	6.95	Fixed	OHIP fee code (SoB): A354, follow-up; assuming 25% of physicians would have this visit in hospital based on expert responses
Foley catheter and drainage bag, consumables	10.53	1	0	Gamma	Follow-up care with indwelling catheters assumed $0 because it is not covered by MOH and is paid out of pocket. Included as a cost of $10.53 in a scenario[f]
Nurse time, wage per minute	0.67[d]	30[d]	20.00[d]	Gamma	Explanation and source[d]
Total monthly costs, indwelling catheter	–	–	26.95		Estimates: $26.95 in the reference case (MOH perspective); $37.48 in a scenario including the device cost
Follow-up: urethroplasty (one-time cost)					
Urethroplasty, procedure cost	9,479.67	1	9,479.67	Gamma	Estimated, case costing initiative 2024 (see Appendix 4)
Physician service, urologist	905.90	1	905.90	Fixed	OHIP fee codes (SoB): S535 ($618.25, assuming no graft, one stage) + S579 ($215.80) + Z606 ($71.85), (S. Neu, MD, oral and email communication, December 13–16, 2024)
Physician service, anesthesiologist, basic units	15.49	6	92.94	Fixed	OHIP fee codes from above, anesthesiology services: 6 basic units
Number of time units in addition to basic	15.49	26	402.74	Fixed	OHIP fee codes from above, anesthesiology services: additional time units for 3–3.5-h surgery
Physician service, total	–	–	1,401.58	NA	Estimate
Total urethroplasty cost		–	**10,881.25**	NA	Estimate

Note: The above-mentioned OHIP fee codes are used for estimation purposes only and represent examples of the fee codes that may be used in clinical practice. They were reviewed during our expert consultation and economic proposal stage and need to be considered a simplifying costing assumption. Also, the average cost of the endoscopic usual care procedure includes all components and consumables.
Abbreviations: DVIU, direct vision internal urethrotomy; ISD, intermittent self-dilatation (self-catheterization); NA, not applicable; MOH, Ontario Ministry of Health; NACRS, National Ambulatory Care Reporting System; OH HTA, Ontario Health Technology Assessment; OHIP, Ontario Health Insurance Plan; SoB, Schedule of Benefits; UC, usual care.

[a]All costs are in 2025 CAD. Some numbers may appear inexact due to rounding. The input parameters related to the physician fees are treated as fixed and were not assigned a distribution in probabilistic analysis. For the rest of the cost inputs, we assigned a gamma distribution.

[b]Markov model used a cycle length of 1 month and some yearly costs were adjusted as appropriate.

[c]DVIU assumed to comprise 50% of all endoscopic management procedures, based on exploration of the use of OHIP fee codes in alignment with the diagnostic codes 598.x/N359 in males (the IntelliHealth OHIP Medical Services database for fiscal year 2022/23[56]).

[d]Estimated nurse wage rate was multiplied by the estimated nurse time spent on the catheter removal. We assumed a registered nurse wage of $40 per hour ($0.67 per min; $40 per hour is a median reported at https://www.jobbank.gc.ca/marketreport/wages-occupation/993/ON, accessed 21 March 2025); we assumed that a nurse would take about 30 min for the removal procedure (20 min on the Foley catheter change and re-insertion, and 10 min for the preparation), yielding a cost of nurse's time of about $20 per procedure.

[e]In a scenario analysis, the costing of self-catheterization with a single-use noncoated intermittent catheter was informed by the data and approach reported in our 2017 report[48]; the list prices of various and available uncoated intermittent catheters (in 2025 CAD) were updated based on available data by Red Leaf Medical (accessed April 01, 2025). An average cost of a noncoated intermittent catheter was estimated at $1.90 (data not shown). Similar to our assumptions in the 2017 report,[48] we assumed the catheter use (i.e., the daily quantity of a noncoated intermittent catheter [single-use]: 5.5 times, multiplied by a 30-day month) and estimated a monthly cost of $341.21.

[f]Source: Online distributors: SciSupply.ca (January 23, 2025): catheter: $6.90 and leg bag: $3.63.

Costing: Procedure With Paclitaxel-Coated Balloon Dilation

Table 13 shows total costs related to one-time use of paclitaxel-coated balloon dilation. We outline the approach and assumptions below:

- **Pre-procedure costs:** As mentioned in the section above, we accounted solely for costs of diagnostic tests that are additional and specific to the paclitaxel-coated balloon procedure, such as use of retrograde urethrogram with or without voiding cystourethrogram (S. Neu, MD, and R. Matta, MD, oral and email communications, December 13, 2024, to August 25, 2025). This work-up was costed under the OHIP fee codes X134 and X135[57]
- **Device costs and consumables:** The cost of a paclitaxel-coated balloon catheter was based on the list price for Optilume, assumed to be $2,800 per device. Additional consumables included an inflation device and a guidewire ($45.00 and $26.99, respectively), yielding a total cost of about $2,872 per person (Laborie Medical Technologies, email communications, January 20 and June 24, 2025)
- **Training:** We assumed no additional costs for physician training because the company provides a short training free of charge (Laborie Medical Technologies, email communication, January 20, 2025). Also, no additional salary renumeration would be needed for training/supervision of fellow surgeons who are conducting the paclitaxel-coated balloon procedure (S. Neu, MD, oral and email communications, December 13 to March 10, 2025)
- **Procedure costs:** We used our prior estimate for the mean cost of usual care endoscopic procedure ($1,089.58 per procedure) and added to it physician service costs to calculate an overall procedure mean cost for paclitaxel-coated balloon dilation. Of note, pre-dilation, which is often required for the paclitaxel-coated balloon procedure, was assumed to be included in the total costs of the procedure and so was not costed separately (S. Neu, MD, oral and email communications, December 13, 2024, to March 10, 2025):
    - *Physician services costs*: No specific physician billing code is currently available for the paclitaxel-coated balloon procedure. We made assumptions based on expert consultation as follows:
        - Physician services claims for paclitaxel-coated balloon dilation included an additional OHIP code E751 ($54.70)[57] that is related to the insertion of chemotherapeutic agent
        - A combination of several OHIP fee codes[57] was used for costing all medical services relevant to paclitaxel-coated balloon dilation: (1) E751 ($54.70, for insertion of chemotherapeutic agent); (2) Z619 ($52.70 for dilatation of stricture, male, general anaesthetic); and (3) Z612 ($250.00 for endoscopic urethral realignment for urethral trauma) (S. Neu, MD, oral and email communications, December 13–16, 2024, and March 10, 2025).
        - In the reference case, we conservatively assumed the cost of anesthesiologist services similar to the one used for usual care urethral dilation procedures (6 basic units and 2 time units for a procedure lasting up to 30 min). We tested this assumption in sensitivity analyses in which we assumed that 50% of the paclitaxel-coated balloon procedures were done

under local anesthesia provided by a urologist surgeon who performs the procedure in an ambulatory setting (Ranno Matta, MD, oral and email communications, March 9 and August 25, 2025)

  - The total mean cost of procedure-related physician services for paclitaxel-coated balloon dilation in the reference case was estimated at $481.32 per person
  - The total procedure mean cost including physician services was estimated at about $1,571 per person

- **Post-procedure costs:** Similar to DVIU**,** after paclitaxel-coated balloon dilation, a Foley catheter would be required (the catheter would be removed 24–48 h post-procedure). We assumed that some proportion of physicians/patients would have 1 additional urologist visit related to the post-procedure follow-up (based on expert consultation, the cost would be $27.80 × 0.25) and we included the cost of consumables paid by the hospital ($10.53) and the nurse time ($20). The estimated post-procedure mean cost was about $37.50 per person
- **Overall mean cost:** The overall mean cost for the paclitaxel-coated balloon dilation procedure, including the additional diagnostic (pre-procedure) work-up, device, consumables, procedure, and post-procedure costs, was estimated at about $4,546 per person
- **Follow-up/monitoring care and additional procedures:** Assumed to be the same as for usual care described in Table 13.

Table 13: Paclitaxel-Coated Balloon Catheter Device and Procedure Costs Used in the Reference Case, Per Person

Variable	Unit cost, $[a]	Quantity	Total cost, $[a]: mean	Distribution	Reference/source
Diagnostic assessment (additional/specific to DCB): a retrograde urethrogram with or without voiding cystourethrogram	X134: 17.95(H) + 6.80(P); X135: 27.50(H) + 13.80(P)	1	66.05	Fixed	OHIP SoB: X134 (retrograde urethrogram) and X135 (cystourethrogram, stress or voiding); S Neu, MD, R Matta, MD, personal communications, December 13, 2024, to March 10, 2025)
DCB device and additional consumables					
DCB Device (Optilume)	2,800.00	1	2,800.00	Gamma	List price (Laborie Medical Technologies, email communication, June 24, 2025)
Catheter-inflation device, consumable	45.00	1	45.00	Gamma	List price (Laborie Medical Technologies, email communications, January 20 and June 24, 2025)
Guidewire, consumable	26.99	1	26.99	Gamma	List price for the Cook guidewire, most common type of guidewire used for the Optilume procedure (Laborie Medical Technologies, email communications, January 20 and June 24, 2025)
Training	0	1	–	NA	No additional charge (Laborie Medical Technologies, email communication, June 24, 2025; S. Neu, MD, oral and email communications, December 13 and Dec 16, 2024, and March 10, 2025)
Pre-dilation for DCB	–	–	–	NA	No additional charge because this cost is included in the cost of services (S. Neu, MD, oral communication, December 13, 2024)
Device and consumable costs, total			2,871.99	NA	Estimate
Procedure with DCB					
Endoscopic usual care procedure (urethral dilation or DVIU)	1,089.58	1	1,089.58	Gamma	Average, all patients, NACRS, Day Surgery, 2022/23, see Appendix 4, Table A11)
Physician service fee, urologist/surgeon	54.70 + 52.70 + 250.00	1	357.40	Fixed	Combination of OHIP codes E751 (insertion of chemotherapeutic agent, $54.70), Z619 (dilatation of stricture, male, $52.70), Z612 (endoscopic urethral realignment for urethral trauma, $250.00) (S. Neu, MD, email and oral communications, December 13, 2024, to March 10, 2025)
Physician service fee, anesthesiologist	15.49[b]	(6+2) × 1[b]	123.92[b]	Fixed	Assumption, 6 basic units plus 2 time units for the procedure lasting ≤ 30 min
Physician service, total			481.32	NA	Estimate
Procedure cost, total			1,570.90	NA	Estimate

Post-procedure					
Physician service, urologist: follow-up with urologist	27.80	0.25	6.95	Fixed	OHIP SoB: A354, follow-up; assuming 25% of physicians would have this visit in hospital, based on expert responses
Foley catheter and drainage bag inserted after the procedure: consumables	10.53	1	10.53	Gamma	Online distributors: SciSupply.ca (January 23, 2025): catheter: $6.90; leg bag: $3.63; assumed to be covered by hospital budget
Nurse time[c]	0.67[c]	30[c]	20.00[c]	Gamma	Explanation and source[c]
Post-Procedure, total			37.48	NA	Estimate
Total cost (pre-, during, and post-procedure one-time cost)			4,546.42	NA	

Note: The above-mentioned OHIP fee codes are used for estimation purposes only and represent examples of the fee codes that may be used in clinical practice. They were reviewed during our expert consultation and economic proposal stage and need to be considered a simplifying costing assumption.

Abbreviations: DCB, paclitaxel-coated balloon catheter; NA, not applicable; NACRS, National Ambulatory Care Reporting System; OHIP, Ontario Health Insurance Plan; SoB, Schedule of Benefits.

[a]All costs are in 2025 CAD. Some numbers may appear inexact due to rounding. The input parameters related to the physician fees are treated as fixed and were not assigned a distribution in probabilistic analysis. For the rest of the cost inputs, we assigned a gamma distribution. The standard error assigned to the cost of the device and consumables was 20% of the mean estimate.

[b]In a scenario, we assumed the use of local anesthesia done by the surgeon, OHIP SoB G224 ($15.55), for the 50% of the time that decreased the cost of physician services from $481.32 to $419.36.

[c]Estimated nurse wage rate was multiplied by the estimated nurse time spent on the catheter removal. We assumed a registered nurse wage of $40 per hour ($0.67 per min; $40 per hour is a median reported at https://www.jobbank.gc.ca/marketreport/wages-occupation/993/ON, accessed March 21 2025). We assumed that a nurse would take about 30 min for the removal procedure (20 min on the Foley catheter change and re-insertion and 10 min for the preparation), yielding a cost of nurse's time of about $20 per procedure.

Costing: Post-Procedure Adverse Events

Based on published sources in this clinical area, we estimated costs related to common adverse events of the procedures as presented in Table 14. Per-person costs were modeled as one-time costs when cohort members resided in a procedure-related (temporary) health state and were costed on a monthly basis (i.e., model cycle) when they were residing in follow-up care health states (e.g., with urethral dilation, self-catheterization, or indwelling catheter, see Figure 5). Therefore, the cost of a potentially chronic condition such as erectile dysfunction was likely underestimated because it was considered a transitory post-procedure adverse event until the cohort member experienced a recurrence of the stricture and was treated with urethral dilation as part of the follow-up monitoring and care. At that point, the cost of treating the condition (e.g., erectile dysfunction) would be incurred on a monthly basis until the end of model simulation. The impact of adverse events on the robustness of reference case results was examined in sensitivity analyses.

Table 14: Adverse Event Post-Procedure Costs Used in the Reference Case, Per Person

Cost input values	Unit cost, $[a]	Quantity	Total cost, $[a]	Reference/source
AEs: endoscopic management with usual care or paclitaxel-coated balloon catheter (one-time)				
Haematuria, mild	87.90 + 2.15	1	90.05	OHIP SoB[57] C005 ($87.90), example code for consultation (visit to GP, R. Matta, MD, personal communications, March 9 to August 25, 2025) Lab fee code: L253, urinalysis ($2.15) (Lab fee schedule)
Dysuria[b]	27.80 + 175.20 [b]	1	203.00[b]	Cost per event, as per approach in Sahakyan et al, 2022[58]: visit to urologist (OHIP fee code: A354) and medication (Mirabegron)[b]
UTI, mild[c]	98.16[c]	1	98.16[c]	Cost per event: Health Quality Ontario, 2019[48]
UTI, serious[d]	522.48 + 106.80 + 14.08	1	643.36	Cost per event included a visit to ED, physician fee, and medication[d]
Urinary retention[e]	269.37[e]	1	269.37[e]	Cost per event, as per approach in Sahakyan et al, 2022[58]
Urinary retention with readmission[f]	1,118.94[f]	1	1,118.94[f]	Cost per event, as per approach in Sahakyan et al, 2022[58] (cost of acute urinary retention)[58]
Erectile dysfunction[g]	318.53 + 522.48 + 106.80[g]	1	947.81[g]	Cost per event included a visit to ER, physician fee and medication
AEs: urethroplasty (one-time)				
Haematuria, mild	87.90 + 2.15	1	90.05	OHIP SoB[57] C005 ($87.90), example code for consultation (visit to GP) (R. Matta, MD, personal communication, March 9, 2025); Lab fee code: L253, urinalysis ($2.15)
UTI, serious[d]	522.48 + 106.80 + 14.08	1	643.36	Cost per event included a visit to ER, physician fee, and medication[d]
Wound infection[h]	522.48 + 126.80 + 6.11[h]		655.39[h]	Cost per event included a visit to ER, physician fee, and medication
Readmission	4,932.00	1	4,932.00	CIHI cost estimator: cost of hospitalization, including physician fees
Erectile dysfunction[g]	318.53 + 522.48 + 106.80[g]	1	947.81[g]	Cost per event included a visit to ER, physician fee, and medication
AEs: self-catheterization or indwelling catheter				
Haematuria, monthly[i]	428.60[i]	1	428.60[i]	Health Quality Ontario, 2019[48]
UTI symptomatic, monthly[c]	98.16[c]	1	98.16[c]	Health Quality Ontario, 2019[48]
Catheter-associated bacteremia and admission to hospital, one time[j]	20,786.29[j]	1	20,786.29[j]	Health Quality Ontario, 2019[48]

Note: The above-mentioned OHIP fee codes are used for estimation purposes only and represent examples of the fee codes that may be used in clinical practice. They were reviewed during our expert consultation and economic proposal stage and need to be considered a simplifying costing assumption.

Abbreviations: AE, adverse events; CI, confidence interval; CIHI, Canadian Institute for Health Information; CPI, consumer price index; ED, emergency department; OHIP, Ontario Health Insurance Plan; SE, standard error; SoB, Schedule of Benefits; UTI, urinary tract infection.

[a]All costs are in 2025 CAD. Some numbers may appear inexact due to rounding. The input parameters were assigned a gamma distribution in probabilistic analysis; SEs determined from 95% CIs based on the published data or assumed to be 20% of the mean only for the estimates directly derived from the literature if SEs were not reported. No distribution assigned to cost of OHIP or medication fee.

[b]Cost per event, as per Sahakyan et al.[58] Visit to urologist was costed using the OHIP fee code: A354 ($27.80) plus cost of medication ($175.20); assumed the use of mirabegron 25 mg 1× daily for 3 mo: $1.46 × 30 × 120 = $175.20. The cost of medication ($1.46) was assumed to be covered by the provincial drug program.[59]

[c]Original cost input value of $78.10 (95% CI: 58.58–97.63)[48] in 2017 CAD was converted to $98.16 (SE:$25.04) in 2025 CAD using the CPI ratio: June 2025 (164.4)/December 2017 (130.8): 1.257.

[d]Cost per event included a visit to the EDR, physician fee, and medication. The original cost for the ED visit was taken from Tarride et al.[60] The original cost input of $463.67 (SD: $369.78, N = 2,129) was reported in 2020/21 CAD and was converted to $522.48 (SE: $9.59) using the CPI ratio of 1.196 (June 2025 [164.4]/December 2020 [137.4]:1.1965). To this cost we added: (1) the cost of the physician fee in ED of $106.80, assuming the OHIP fee code: H055 (A888), with no premium included; and (2) the cost of medication: oral ciprofloxacin 2× daily for 14 d at $0.503 per tablet.[59]

[e]Original cost input value of $182.00 (95% CI: $137–$228)[58] in 2017 CAD was converted to $269.37 (SE: $68.72) in 2025 CAD using the CPI ratio 1.257.

[f]Original cost input value of $756.00 (95% CI: $567–$945)[58] in 2017 CAD was converted to $1,118.94 (SE: $285.44) in 2025 CAD using the CPI ratio 1.257.

[g]Cost per event included a visit to the ED, physician fee, and medication. Medication was costed as per Sahakyan et al[58]: Apo-Sildenafil, 50 mg Tab, 12 tablets for 3 mo: $8.848 × 12 × 3 = $318.53, assuming coverage by the provincial drug program.[59] The original cost for an ED visit was taken from Tarride et al.[60] The original cost input of $463.67 (SD: $369.78, N = 2,129) was reported in 2020/21 CAD and was converted to $522.48 (SE: $9.59) using the CPI ratio of 1.196 (June 2025 [164.4]/December 2020 [137.4]:1.196). To this cost, we added the cost of physician fees in the ED of $106.80, assuming the OHIP fee code H055 (A888), with no premium included.

[h]Cost per event included a visit to the ED, physician fee, and medication. The original cost for an ED visit was taken from Tarride et al.[60] The original cost input of $463.67 (SD: $369.78, N = 2,129) was reported in 2020/21 CAD and converted to $522.48 (SE: $9.59) using the CPI ratio of 1.196 (June 2025 [164.4]/December 2020 [137.4]:1.196). To this cost, we added the cost of physician fees in the ED of $106.80, assuming the OHIP fee code H055 (A888), with no premium included, and a fee of $20 for the wound drainage (OHIP code Z080, local anesthetic). Medication was costed as per Sahakyan et al,[58] assuming use of oral antibiotics and coverage by the provincial drug program: Trimethoprim-Sulfamethoxazole (TMP-SMX), 2× daily, $0.2184 per tablet for 14 d,[59] yielding $6.11 for the medication (R. Matta, MD, email communications, March and August, 2025).

[i]Original cost input value of $341.00 (95% CI:$255.75–$426.25) in 2017 CAD[48] was converted to $428.60 (SE: $109.34) in 2025 CAD using the CPI ratio 1.257.

[j]Original cost input value of $16,538.00 (95% CI: $12,403–$20,672) in 2017 CAD[48] was converted to $20,786.29 (SE: $5,302.63) in 2025 CAD using the CPI ratio 1.257.

Internal Validation

The secondary health economist conducted formal internal validation. This process included testing the mathematical logic of the model, checking for errors, and ensuring the accuracy of parameter inputs and equations.

Equity Considerations

Due to limited data, we did not conduct a cost–utility analysis or an equity-related subgroup analysis. We explored the impact of several factors that may affect inequity in access on the reference case results (see more details in Scenario Analysis section), for instance:

- Participation or acceptance of paclitaxel-coated balloon dilation and usual care (100% in the reference case, Table 10)
- Age at baseline (45 years in the reference case)
- Acceptance of urethroplasty (mean: 90%) and wait time for urethroplasty (mean 130 days in the reference case, Table 10)
- Costs of intermittent self-catheterization or indwelling catheters that are paid out of pocket by patients ($341.21 per month per person and $10.53 per month per person, respectively, see Table 12)
- Cost of the device (Table 13)

Analysis

Our reference case and sensitivity analyses adhered to the Canada's Drug Agency (CDA) guidelines[40] when appropriate. The reference case represents the analysis with the most likely set of input parameters and model assumptions.

We calculated the reference case estimates by running 10,000 simulations in a probabilistic analysis that simultaneously captured the uncertainty in all parameters that were expected to vary. We set distributions for variables within the model. The probabilistic analyses were conducted using TreeAge Pro (Healthcare Version 2025.2.0).[61] We calculated mean costs with credible intervals and mean probabilities (effects) for recurrence (following the endoscopic management) and safety outcomes with credible intervals for each intervention assessed. We also calculated the mean incremental costs with credible intervals, incremental effects with credible intervals, and whenever appropriate, the incremental cost-effectiveness ratios (ICERs) of paclitaxel-coated balloon dilation versus usual care.

The results of the probabilistic analysis were presented in a scatter plot on a cost-effectiveness plane and/or in a cost-effectiveness acceptability curve. We used a range of willingness-to-pay (WTP) thresholds up to $100,000 per effectiveness outcome averted to present uncertainty in the cost-effectiveness results. Because there is no established WTP for the cost-effectiveness analysis, we did not make any conclusion on the cost-effectiveness of the intervention versus alternatives at a pre-specified WTP value; however, we examined the probability of the paclitaxel-coated balloon intervention being cost saving or optimal using a WTP of $0 per a urethral stricture recurrence avoided, and estimated incremental net monetary benefit (INB, expressed in CAD) at that WTP value. An INB value greater than $0 indicated that the intervention was cost-effective or cost-saving at the given WTP. We also conducted one-way sensitivity analyses by varying specific model parameters to examine their impact on the reference case results and, when possible, estimated a threshold value (breakeven point) at which the intervention was cost neutral or cost-saving, compared to usual care. We used a tornado diagram to present the results of the one-way deterministic sensitivity analyses.

Scenario Analyses

We conducted numerous scenario analyses to explore uncertainty in:

- Parameter assumptions related to the effectiveness of paclitaxel-coated balloon dilation
- Method and structural model assumptions and overall parameter uncertainty (cost and probability inputs related to the usual care or intervention)
- Value of urethroplasty (compared with the paclitaxel-coated balloon intervention)

Scenarios: Uncertainty in Effectiveness of Paclitaxel-Coated Balloon Dilation

As shown in Table 15, we conducted a scenario analysis pertinent to the effectiveness of paclitaxel-coated balloon dilation on urethral strictures at the bulbar site, as reported in the ROBUST III trial.[25] We also examined the impact of decreasing the effectiveness of paclitaxel-coated balloon dilation by applying a multiplier on an estimated reference case distribution (Table 11); this resulted in decreasing a non-recurrence of urethral strictures following the endoscopic procedure up to 45% over time and at 5 years, compared with the rates in the reference case.

Table 15: Scenario Analyses – Effectiveness of Paclitaxel Coated Balloon Dilation

Scenarios	Reference case: mean[a,b]	Scenario: mean[a,b]	Sources
1 Scenario: Effectiveness of paclitaxel-coated balloon dilation, freedom from reintervention, bulbar urethral strictures			Assumptions for the bulbar site made on ROBUST III RCT data[25]
At 12 months, not retreated	83.2%	88.3%	
At 24 months, not retreated	78.5%	82.0%	
3 Scenarios: Multiplier effectiveness factor, to increase the recurrence rate over time (3 scenarios)	1× Reference case distribution	2× 2.5× Threshold (i.e., INB = 0)	Estimated, multiplying reference case distribution (Table 11) with the multilier factor that decreased the effectiveness, resulting in higher recurrence rates compared to the reference case

Abbreviations: INB, incremental net monetary benefit; RCT, randomized controlled trial.

[a]Standard errors were estimated where data was available. Estimates for the usual care remained the same as in the reference case (Table 10: 21.7%).

[b]Beta distributions were assigned to the probability estimates in probabilistic analysis.

Scenarios: Uncertainty in Assumptions on Methods, Model Structure, and Clinical and Cost Parameters

We conducted a set of one-way scenarios including threshold analyses to examine the influence of various model inputs, such as starting age, time horizon, acceptance of endoscopic and urethroplasty procedures, costs of follow-up procedures paid out of pocket, and use of local anesthesia and endoscopic suite settings for the paclitaxel-coated balloon procedure. These analyses are described in Table 16.

Table 16: Probabilistic Scenarios and Threshold Analyses – Method, Structural and Parameter Assumptions

Parameters	Reference case	Scenarios[a]
Starting age	45 y	3 scenarios: 55, 65, and 75 y
Time horizon	5 y	5 scenarios: 1, 2, 3, and 4 y and threshold analysis for time horizon
Discount rate	1.5%	2 scenarios: discount rate on both outcomes – 0% and 5%
Participation: probability of accepting the initial treatment (endoscopic management)	1.00	2 scenarios: 50% and 75%
Probability of accepting treatment with urethroplasty	90%	3 scenarios: 50% and 75% and threshold analysis for this parameter
Waiting time for urethroplasty	130 d (30–230 d)	3 scenarios: 30 and 720 d and threshold analysis for this parameter

Parameters	Reference case	Scenarios[a]
Effectiveness of urethroplasty: probability of recurrence at 10 years	72.2% (see Table 10)	2 scenarios: muitipler factor of 0.5× lower and 2× higher
Probability of using urethral dilation, ISD, or indwelling catheters, follow-up care	80% in Dirischlet (80;15;5)	1 scenario: 100% (i.e., use of ISD and indwelling catheters = 0)
Probability of indwelling catheters, follow-up care	5% in Dirischlet (80;15;5)	1 scenario: 25% (use of ISD = 15% and urethral dilation = 60%)
Costs of ISD or indwelling catheters	$0 (Ministry perspective, no coverage)	1 scenario: fully paid; i.e., ISD = $341.21 or indwelling catheters = $10.53 per month
Use of local anesthesia in the paclitaxel-coated balloon procedure (no change in the overall procedure costs)	None (0%)	1 scenario: 50%
Change of setting towards ambulatory – endoscopy suite setting: use of local anesthesia in the paclitaxel-coated balloon procedure and reduction of the procedure costs	No local anesthesia (0%) and an average procedure cost of endoscopic procedures ($1,089.58; Tables 12 and 13)	1 scenario: 50% use local anesthesia and those who use local anesthesia have the cost of dilation with endoscopic suite ($459.94, see Appendix 4)

Abbreviation: ISD, intermittent self-catheterization.
[a]Probabilistic analyses done (except for threshold analyses, which were deterministic in nature). Only the value(s) of indicated parameters change, while the rest remained same as in the reference case.

Next, we varied the following cost and probability input parameters and used tornado diagrams to show their impact on the reference case cost-effectiveness results:

- **Cost inputs**:
  - Device, reference case: $2,800 (low: $1,000 to high: $6,000)
  - Endoscopic procedure: $1,089 (low: $500 to high: $2,200)
  - Urethroplasty: $10,881 (low: $5,000 to high: $22,000)
  - Adverse events
    - Hematuria procedure-specific: $90.05 (low: $50 to high: $200)
    - Hematuria intermittent self-catheterization (ISD)–specific: $429 (low: $250 to high: $900)
    - UTI procedure-specific, mild: $98 (low: $50 to high: $200)
    - UTI procedure-specific, serious: $643 (low: $300 to high: $1,300)
    - UTI ISD-specific: $98 (low: $50 to high: $200)
    - Dysuria: $203 (low: $100 to high: $400)
  - Urinary retention (incontinence)
    - Procedure-specific, mild: $269 (low: $130 to high: $520)
    - Procedure-specific, serious: $1,119 (low: $500 to high: $2,500)

  - Bacteraemia due to catheterization: $20,786 (low: $10,000 to high: $42,000)
  - Erectile dysfunction: $948 (low: $500 to high: $2,000)
  - Wound infection following the surgery: $655 (low: $300 to high: $1,300)
  - Readmission after surgery: $4,932 (low: $2,500 to high: $10,000)
- **Probability inputs** related to main adverse events following endoscopic, catheterization, or surgical procedures
  - Hematuria, usual care or paclitaxel procedure, reference case: 0.021/0.038 (low: 0.01 to high: 0.07)
  - Hematuria, ISD-related: 0.004 (low: 0.00 to high: 0.1)
  - Hematuria, surgery-related: 0.02 (low: 0.00 to high: 0.04)
  - UTI, usual care or paclitaxel procedure total: 0.104/0.114 (low: 0.01 to high: 0.30)
  - UTI ISD-related: 0.195 (low: 0.00 to high: 0.50)
  - UTI surgery-related: 0.03 (low: 0.01 to high: 0.10)
  - Dysuria, usual care or paclitaxel procedure: 0.02/0.09 (low: 0.01 to high: 0.20)
  - Urinary retention
    - Usual care or paclitaxel procedure, total: 0.08/0.08 (low: 0.01 to high: 0.20)
    - Usual care or paclitaxel procedure, readmission [conditional]: 0.75/NA (low: 0.00 to high: 1.00)
  - Bacteraemia due to catheterization: 0.04 (low: 0.00 to high: 0.07)
  - Erectile dysfunction
    - Usual care or paclitaxel procedure: 0.021/0.00 (low: 0.01 to high: 0.05)
    - Surgery-related: 0.05 (low: 0.01 to high: 0.10)
  - Wound infection following the surgery: 0.01 (low: 0.00 to high: 0.05)
  - Readmission after the surgery: 0.03 (low: 0.00 to high: 0.06)

Additional Scenarios: Urethroplasty

Based on expert consultation (S. Neu, MD, and R. Matta, MD, email and oral communications, March 10 to August 25, 2025), additional probabilistic scenarios were done to address urethroplasty as a separate comparator or with an off-label use of paclitaxel-coated balloon dilation following urethroplasty.

In these scenarios, we made structural changes to the reference case model. The main effectiveness outcome that we evaluated was a recurrence after all stages of treatment, including recurrence after the surgical procedure, and not only after the first endoscopic procedure.

In the first scenario, which examined urethroplasty as a direct comparator to paclitaxel-coated balloon dilation, we differentiated several urethroplasty strategies based on the acceptance rate of the surgical procedure. These were compared to the usual care and paclitaxel-coated balloon dilation strategies:

- Urethroplasty, accepted by 100% of patients with immediate access to it (i.e., no wait time)
- Urethroplasty, accepted by 75% of patients with immediate access to it (i.e., no wait time)

Similar to the reference case model assumptions, people who did not get the surgery would have 3 follow-up care options, including monthly monitoring (with urethral dilation, self-catheterization, or indwelling catheter).

In the second scenario, which explored off-label use of paclitaxel-coated balloon dilation, we assumed that the only use of paclitaxel-coated balloon dilation would occur after urethroplasty in those who fail the surgery. Given this structure, all patients had to have the surgery (i.e., assuming 100% access). We developed 2 additional off-label use strategies that were compared with the usual care and paclitaxel-coated balloon dilation strategies:

- One did not allow for a second use of urethroplasty following the recurrence from paclitaxel-coated balloon dilation
- Another allowed for a second use of urethroplasty following the recurrence from paclitaxel-coated balloon dilation

Results

Reference Case Analysis

Table 17 provides the results of the reference case analysis from the perspective of the Ontario Ministry of Health. Over the 5-year time horizon, urethral dilation with a paclitaxel-coated balloon catheter was less costly and more effective compared with usual care.

The mean total costs for paclitaxel-coated balloon dilation and usual care were $7,189.47 and $8,665.91 per person, respectively. Paclitaxel-coated balloon dilation was associated with cost savings of about $1,476.44 per person over 5 years (95% Credible Interval [CrI]: −$3,217.15 to $112.40), compared with usual care. The 95% CrI around the point estimate is wide, and ranges from cost savings to a cost increase, which suggests substantial uncertainty in the amount of cost savings that could be achieved with paclitaxel-coated balloon dilation.

Over the same period, paclitaxel-coated balloon dilation reduced urethral stricture recurrence by 69% after the initial procedure, as defined by the clinical outcome freedom from reintervention (recurrence reduction, 95% CrI: 68%–70%). Undiscounted effectiveness estimates with the cost-effectiveness results are presented in Appendix 5.

Table 17: Reference Case Analysis Results: Cost-Effectiveness Outcomes

Strategy	Total costs, $[a] mean (95% CrI)	Incremental cost, $[a,b,c] mean (95% CrI)	Total effects, probability of recurrence[c,d,e] mean (95% CrI)	Incremental effect[c,d,e] mean (95% CrI)	ICER[c,f]
Usual care	8,665.91 (7,315.49; 10,793.27)		0.9882 (0.9879; 0.9885)		
Paclitaxel-coated balloon dilation	7,189.47 (6,072.26; 8,507.80)	−1,476.44 (−3,217.15; 112.40)	0.2984 (0.2901; 0.3069)	−0.6898 (−0.6980; −0.6813)	Dominant: more effective and less costly

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio.

[a]Incremental cost = average cost (paclitaxel-coated balloon dilation) − average cost (usual care). All costs are expressed in 2025 CAD (discount rate: 1.5%).

[b]Negative costs indicate savings.

[c]Results may appear inexact due to rounding.

[d]Incremental effect = average effect (paclitaxel-coated balloon dilation) − average effect (usual care). The effectiveness outcome was defined as a recurrence after initial endoscopic management (i.e., reintervention needed at 5 years, as determined by the clinical outcome: freedom from reintervention). Negative sign indicates reduction in the probability of the recurrence at 5 years (positive outcome).

[e]Estimates were discounted (rate: 1.5%).

[f]Incremental cost-effectiveness ratio was calculated as a ratio by dividing the mean incremental cost with the mean incremental effect; it is for example expressed as additional cost gained or averted per additional unit of effect.

Table 18 presents comparisons between paclitaxel-coated balloon dilation and usual care for other outcomes such as adverse events (AEs) following the initial or next endoscopic procedure, follow-up treatment options after unsuccessful first procedure, and costs associated with AEs.

We estimate statistically significant increases in the likelihood of hematuria and dysuria of about 1.7% and 6.8% on average, respectively, and a nonsignificant increase in the likelihood of urinary tract infections of about 1% after paclitaxel-coated balloon dilation compared with usual care. However, there was a statistically significant decrease in costlier AEs, such as acute urinary retention or erectile dysfunction, and a substantial decrease in all AEs that occurred in people who were not successfully treated with the first procedure and needed additional retreatment with endoscopic or other options (self-catheterization or indwelling catheters). As a result, with regard to the cost of AEs altogether, paclitaxel-coated balloon dilation resulted in per-person cost savings.

We also estimate a reduction in the need for follow-up procedures in people initially treated with paclitaxel-coated balloon dilation compared with those treated with usual care. For instance, the use of urethroplasty was reduced by about 23.8% over 5 years, which could indicate that paclitaxel-coated balloon dilation may delay a need for this invasive and costly surgery. Also, we estimated a reduction in the use of urethral dilation procedures in people with recurring strictures of about 36.5% over 5 years. These results provide additional insights and an explanation related to the overall (total) mean savings with paclitaxel-coated balloon dilation showed in the reference case analysis (Table 17).

Table 18: Reference Case Analysis Results for Safety and Other Outcomes

Outcome	Usual care	Paclitaxel-coated balloon dilation	Difference: paclitaxel-coated balloon dilation – usual care[a]
Post first procedure AE: hematuria, *P*, mean (95% CrI)[b,c]	0.021 (0.015–0.027)	0.038 (0.030–0.046)	0.017 (0.007–0.027)
Post first procedure AE: dysuria, *P*, mean (95% CrI)[b,c]	0.021 (0.015–0.027)	0.089 (0.072–0.107)	0.068 (0.050–0.087)
Post first procedure AE: UTI, *P*, mean (95% CrI)[b,c]	0.104 (0.079–0.132)	0.114 (0.093–0.137)	0.010 (−0.025 to 0.044)
Post first procedure AE: urinary retention, *P*, mean (95% CrI)[b,c]	0.083 (0.063–0.106)	0.076 (0.061–0.092)	−0.007 (−0.034 to 0.018)
Post first procedure AE: erectile dysfunction, *P*, mean (95% CrI)[b,c]	0.021 (0.027–0.016)[d]	0.00	−0.021 (−0.027 to −0.016)[d]
AEs, first endoscopic procedure: total, *P*, mean (95% CrI)[b,c]	0.250 (0.216–0.287)	0.316 (0.284–0.351)	0.066 (0.017–0.115)
AEs, second endoscopic procedure: total, *P*, mean (95% CrI)[c,e]	1.00[f]	0.732 (0.388–1.00[f])	−1.00[f]
Follow-up procedures for the recurrence after first procedure:			
Urethroplasty (surgery), *P*, mean (95% CrI)[c]	0.342 (0.214–0.608)	0.104 (0.065–0.185)	−0.238 (−0.048 to −0.149)
Urethral dilation, *P*, mean (95% CrI)[c]	0.525 (0.307–0.650)	0.160 (0.094–0.199)	−0.365 (−0.453 to −0.215)
ISD, *P*, mean (95% CrI)[c]	0.098 (0.048–0.157)	0.030 (0.015–0.048)	−0.068 (−0.109 to −0.033)
Indwelling catheters, *P*, mean (95% CrI)[c]	0.033 (0.010–0.069)	0.010 (0.003–0.021)	−0.023 (−0.048 to −0.007)
AEs: total cost, $, mean (95% CrI)[g]			
AEs, first endoscopic procedure, $, mean (95% CrI)	111.321 (76–159)	63.746 (50–80)	−47.574 (−89 to −17)
AEs, second endoscopic procedures, $, mean (95% CrI)	1,373.845 (593–2,494)	358.170 (154–649)	−1,015.675 (−1,843 to −440)

Note: A total number of AEs may include other AEs not presented in the table above. Reductions in the costs of all AEs following the first endoscopic procedure are a result of reduction of AEs with higher costs. Because these estimates are based on simplifying modeling assumptions, they need to be interpreted with caution.

Abbreviations: AE, adverse event; CrI, credible interval; ISD, intermittent self-catheterization; UTI, urinary tract infection.

[a]Negative values indicate reductions or cost savings.

[b]AEs after the first (initial) endoscopic dilation procedure (at the beginning of model simulation).

[c]Undiscounted effectiveness outcome values presented in the table.

[d]Modeled estimates, based on reported input data.

[e]AEs associated with next second dilation procedures in people who failed the first endoscopic procedure and did not choose surgical option.

[f]The probability is based on counting AEs and is rounded to 1 because people in usual care had multiple AEs from the procedures (2.809, 95% CI: 1.479–4.331). The estimate for the paclitaxel-coated balloon dilation arm was 0.732 (0.388–1.133) and the estimate for the difference was −2.077 (−3.2 to −1.09), which indicated multiple AEs. Their 100% reduction was rounded to 1.00.

[g]Expressed in 2025 CAD, discounted at a rate: 1.5%.

Figure 6 presents the results of our probabilistic analysis in a cost-effectiveness acceptability curve and Figure 7 presents them as a scatter plot on a cost-effectiveness plane. Urethral dilation with the paclitaxel-coated balloon catheter was cost-saving at a probability of 96.7% (WTP of $0 per recurrence avoided) and higher compared with usual care across a wide range of willingness to pay values.

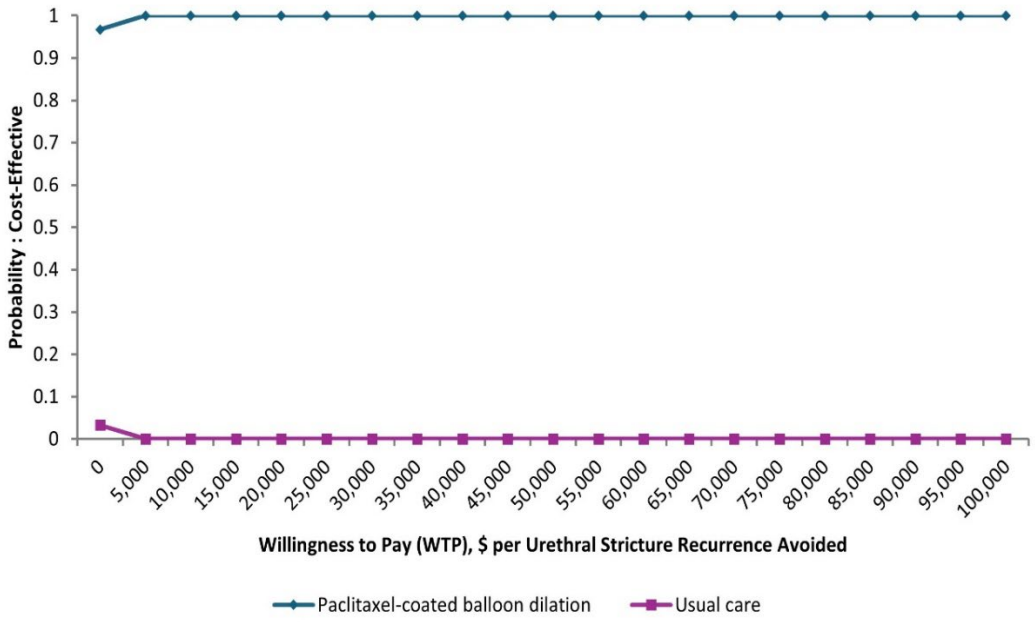

Figure 6: Cost-Effectiveness Acceptability Curve: Paclitaxel-Coated Balloon Dilation Versus Usual Care

A cost-effectiveness acceptability graph showing the results of the probabilistic analysis. Paclitaxel-coated balloon dilation was associated with a very high probability of being cost-saving compared to usual care because it was associated with considerable cost savings.

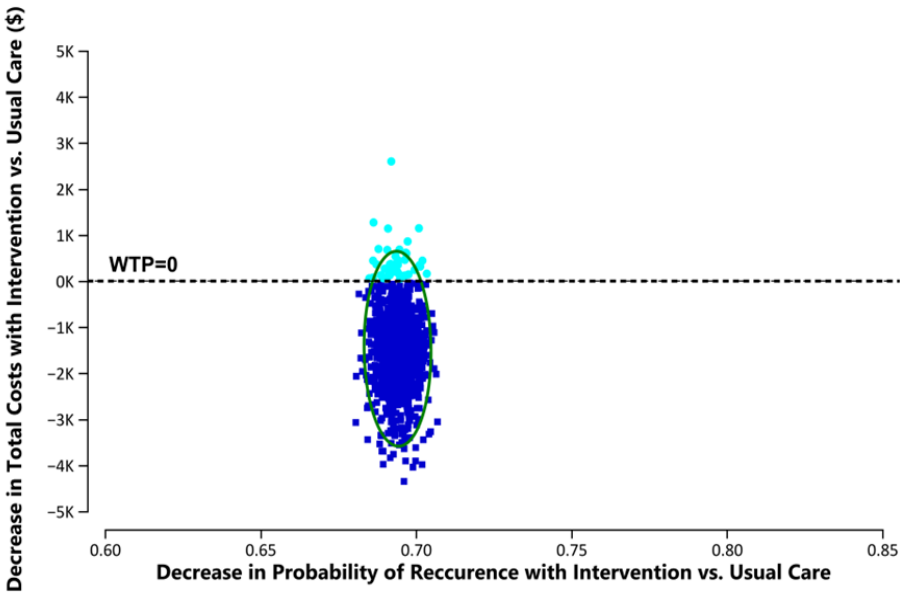

Figure 7: Scatter Plot of Probabilistic Results at a Willingness-to-Pay Value of $0 per Avoided Recurrence, Paclitaxel-Coated Balloon Dilation Versus Usual Care

Abbreviation: WTP, willingness to pay.
A scatter plot of probabilistic results showing the findings from the 10,000 model iterations. Treatment with paclitaxel-coated balloon dilation was found to be more effective and less costly than usual care about 97% of the time at a WTP of $0 per stricture recurrence avoided.

Scenario Analyses

Scenarios: Uncertainty in the Effectiveness of Paclitaxel-Coated Balloon Dilation

As shown in Table 19, cost savings with paclitaxel-coated balloon dilation were higher for urethral strictures at the bulbar site because of the greater effectiveness of the intervention (i.e., greater reduction in the recurrence) shown for this site in the ROBUST III trial.[25] Consequently, the probability that this intervention is the optimal and cost saving strategy was slightly higher compared with the reference case (98.6% vs. 97.7%).

In scenarios that examined the impact of reduction of the effectiveness of paclitaxel-coated balloon dilation, we showed that if we assumed a 2.5 times higher rate of recurrence with the intervention over time (i.e., a no-recurrence rate of about 67% at 12 months and about 40% at 5 years), then the incremental effectiveness would still be lower with the intervention (a reduction of 40%), but there would be no savings (incremental cost of about $371.2), resulting in an ICER of an additional $928 per recurrence avoided. In this scenario, the probability of the intervention being a cost-effective (optimal) strategy at a WTP of $0 per recurrence avoided was very low (28.8%). Figure 8 presents additional results of the threshold analysis on the effectiveness parameter and suggests that the reduction of recurrence needs to be about 2.07 times smaller over time compared with that in the reference case for INB to become zero (i.e., breakeven point between the 2 strategies, meaning no cost savings with paclitaxel-coated balloon dilation).

Table 19: Scenario Analysis Results: Effectiveness of Paclitaxel-Coated Balloon Dilation

Scenario	Average total cost, $[a]	Incremental cost, $[b,c]	Average total effect[d]	Incremental effect[c,d,e,f]	ICER ($ per recurrence)	INB (WTP = 0), $[g]	Paclitaxel-coated balloon dilation being optimal (cost-saving)
Reference case	UC: 8,665.91 DCB: 7,189.47	−1,476.44	UC: 0.99 DCB: 0.30	−0.69	Dominant	INB > 0: 1476.44	96.72%
1: Effectiveness of paclitaxel-coated balloon dilation on bulbar urethral strictures	UC: 8,665.91 DCB: 6841.19	−1,824.70	UC: 0.99 DCB: 0.28	−0.71	Dominant	INB > 0: 1,824.91	98.63%
2: Decreasing effectiveness of paclitaxel-coated balloon dilation by 2×	UC: 8,665.91 DCB: 8517.99	−147.91	UC: 0.99 DCB: 0.51	−0.48	Dominant	INB > 0: 147.91	58.62%
3: Decreasing effectiveness of paclitaxel-coated balloon dilation by 2.5×	UC: 8,665.91 DCB: 9037.08	371.17	UC: 0.99 DCB: 0.59	−0.40	$928 per recurrence avoided	INB < 0: −371.17	28.81%

Abbreviations: DCB, paclitaxel-coated balloon dilation; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit; UC, usual care; WTP, willingness to pay.

[a]All costs in 2025 CAD.

[b]Incremental cost = average cost (strategy: paclitaxel-coated balloon dilation) − average cost (strategy: usual care).

[c]Negative costs indicate savings.

[d]Effectiveness expressed as the probability of recurrence of urethral strictures, annual discount rate: 1.5%.

[e]Results may appear inexact due to rounding.

[f]Incremental effect = average effect (strategy: ppaclitaxel-coated balloon dilation) − average effect (strategy: usual care) .

[g]Incremental net monetary benefit was calculated at a WTP of $0 per recurrence using the following formula: incremental effect × WTP – incremental cost. When INB is > 0, then the intervention is considered cost-effective and, in this case, cost saving.

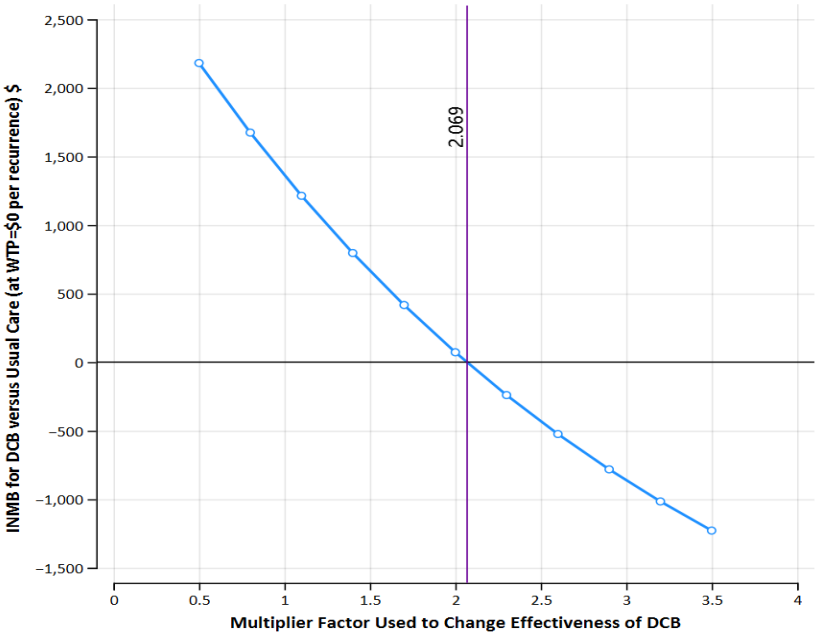

Figure 8: Threshold Analysis: Reduction of the Effectiveness of Paclitaxel-Coated Balloon Dilation and Cost-Savings

Abbreviations: DCB, paclitaxel-coated balloon dilation; INMB, Incremental net monetary benefit; WTP, willingness to pay.
The threshold analysis for changes in the effectiveness of paclitaxel-coated balloon dilation (x-axis) against the incremental net monetary benefit (y-axis). The threshold line is 2.069. It means that the reduction of urethral stricture recurrence needs to be about 2.07 times smaller compared with that in the reference case for the incremental net monetary benefit to be zero, resulting in no cost savings with the intervention (i.e., the breakeven point).

Scenarios: Uncertainty in Assumptions on Methods, Model Structure, and Clinical and Cost Parameters

Table 20 provides a summary of the results of various scenario analyses. The intervention with paclitaxel-coated balloon dilation remained cost saving in all but in 1 scenario that was related to the duration of the time horizon. When we assumed a 1-year time horizon for our analysis, the treatment with paclitaxel-coated balloon dilation was associated with a reduction of recurrence of about 59%, but also an additional $1,053, yielding an ICER of about additional $1,796 per recurrence avoided. The probability of the intervention being cost saving (WTP = 0) was very low, about 10%. However, as the model time horizon increased, the probability of the intervention being cost saving became higher: about 62%, 77%, and 90% after 2, 3, and 4 years, respectively.

In addition, compared with the reference case, the intervention was more likely to be cost saving when we assumed the following:

- No discounting (Scenario 3A): 97.43% (vs. 96.72% in reference case)
- Shorter waiting time for the surgery (30 days, Scenario 6A): 100%
- 2 times higher effectiveness of the surgery on the recurrence (Scenario 7B): 97.28%
- Higher use of indwelling catheters as part of the follow-up care (Scenario 9): 99.90%

- Inclusion of the costs for intermittent and indwelling catheters paid by patients (Scenario 10): 99.90%
- Decreased costs of anesthesia in terms of use of local anesthesia by a surgeon in 50% of the paclitaxel-coated balloon dilation procedures (Scenario 11): 97.24%
- Decreased costs of the paclitaxel-coated balloon dilation procedure (use of local anesthesia in 50% of the procedures, with smaller endoscopic suite procedure costs, Scenario 12): 98.87%

The intervention was substantially less likely to be cost saving than the reference case when we assumed:

- A shorter (i.e., 1–3-year) time horizon (Scenarios 2A–2C): 9.95% to 76.71%
- A smaller (50%) acceptance (uptake) rate of the surgery (urethroplasty) due to recurrence after endoscopic management (Scenario 5A): 73.31%
- A longer waiting time for the surgery (720 days, Scenario 6B): 53.33%
- 100% use of urethral dilation as part of follow-up care procedures due to recurrence after endoscopic management (Scenario 8): 78.43%

Threshold values were found for the following parameters, at which point the intervention became cost neutral (INB = 0):

- A time horizon (Scenario 2) of 1.88 years (vs. 5 years in the reference case)
- An acceptance (or uptake) rate of the surgery due to recurrence after endoscopic management (Scenario 5) of 0.244 (vs. 0.90 in the reference case)
- Wait time for the surgery (Scenario 6) of 869 days (vs. 130 days in the reference case)

Table 20: Scenario Analysis Results: Structural, Method, and Parameter Assumptions

Scenario	Average total cost, $[a]	Incremental cost, $[b,c]	Average total effect[a]	Incremental effect[c,d,e,f]	ICER	INB (WTP = 0), $[g]	Paclitaxel-coated balloon dilation being optimal (cost-saving), %
Reference case	UC: 8,665.91 DCB: 7,189.47	−1,476.44	UC: 0.998 DCB: 0.298	−0.689	Dominant	INB > 0: 1,476.44	96.72%
1A: Starting age, 55 y	UC: 8,605.34 DCB: 7,167.77	−1,437.57	UC: 0.986 DCB: 0.297	−0.688	Dominant	INB > 0: 1,437.57	96.41%
1B: Starting age, 65 y	UC: 8,511.13 DCB: 7,124.41	−1,386.72	UC: 0.981 DCB: 0.294	−0.687	Dominant	INB > 0: 1,386.72	95.86%
1C: Starting age, 75 y	UC: 8,254.38 DCB: 7,006.28	−1,248.10	UC: 0.981 DCB: 0.294	−0.681	Dominant	INB > 0: 1,248.10	94.35%
2A: Time horizon, 1 y	UC: 4,242.47 DCB: 5,296.12	−1,053.64	UC: 0.730 DCB: 0.144	−0.586	$1,796 per recurrence avoided	INB < 0: −1,053.64	9.95%
2B: Time horizon, 2 y	UC: 6,248.58 DCB: 5,903.86	−344.73	UC: 0.988 DCB: 0.226	−0.762	Dominant	INB > 0: 344.73	61.66%
2C: Time horizon, 3 y	UC: 7,060.66 DCB: 6,442.79	−617.87	UC: 0.988 DCB: 0.283	−0.705	Dominant	INB > 0: 617.87	76.71%
2D: Time horizon, 4 y	UC: 7,867.55 DCB: 6,848.16	−1,019.39	UC: 0.988 DCB: 0.297	−0.691	Dominant	INB > 0: 1,019.39	90.29%
3A: Discount rate, 0%	UC: 8,861.81 DCB: 7,274.87	−1,586.95	UC: 0.998 DCB: 0.304	−0.694	Dominant	INB > 0: 1,586.95	97.43%
3B: Discount rate, 5%	UC: 8,249.00 DCB: 7,008.70	−1,240.31	UC: 0.966 DCB: 0.286	−0.680	Dominant	INB > 0: 1,240.31	94.27%
4A: Participation, initial procedure, 50%	UC: 7,029.42 DCB: 6,291.21	−738.22	UC: 0.494 DCB: 0.149	−0.345	Dominant	INB > 0: 738.22	96.72%
4B: Participation, initial procedure, 75%	UC: 7,847.67 DCB: 6,740.34	−1,107.33	UC: 0.741 DCB: 0.223	−0.517	Dominant	INB > 0: 738.22	96.72%
5A: Accepting treatment with urethroplasty, 50%	UC: 7,150.29 DCB: 6,709.11	−441.18	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 441.18	73.31%
5B: Accepting treatment with urethroplasty, 75%	UC: 7,958.24 DCB: 6,965.18	−993.06	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 993.06	90.80%
6A: Waiting time for urethroplasty, 30 d	UC: 12,218.34 DCB: 8,315.39	−3,902.95	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 3,902.95	100.00%
6B: Waiting time for urethroplasty, 720 d	UC: 6,573.15 DCB: 6,526.08	−46.97	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 46.97	53.33%
7A: Effectiveness of urethroplasty on recurrence, 0.5× lower	UC: 8,573.24 DCB: 7,169.77	−1,403.47	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 1,403.47	96.28%
7B: Effectiveness of urethroplasty, 2× higher	UC: 8,826.49 DCB: 7,223.92	−1,602.57	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 1,602.57	97.28%

Scenario	Average total cost, $[a]	Incremental cost, $[b,c]	Average total effect[a]	Incremental effect[c,d,e,f]	ICER	INB (WTP = 0), $[g]	Paclitaxel-coated balloon dilation being optimal (cost-saving), %
8: Follow-up care, urethral dilation 100%	UC: 7,550.45 DCB: 6,902.66	−647.80	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 647.80	78.43%
9: Follow-up care, indwelling catheter 25%, urethral dilation 60% and ISD 15%	UC: 10,784.49 DCB: 7,734.13	−3,050.36	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 3,050.36	99.90%
10: Inclusion of costs of ISD or indwelling catheters	UC: 10,416.61 DCB: 7,639.27	−2,777.33	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 2,777.33	99.90%
11: Use of local anesthesia in 50% of DCB procedures	UC: 8,665.91 DCB: 7,118.54	−1,547.36	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 1,547.36	97.24%
12: Setting: Use of local anesthesia in 50% of DCB procedures with smaller endoscopic suite procedure costs	UC: 8,665.91 DCB: 6,803.79	−1,862.11	UC: 0.988 DCB: 0.298	−0.689	Dominant	INB > 0: 1,862.11	98.87%

Abbreviations: DCB, paclitaxel-coated balloon dilation; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit; ISD, intermittent self-catheterization; UC, usual care; WTP, willingness to pay.

[a]All costs in 2025 CAD.

[b]Incremental cost = average cost (strategy: DCB) − average cost (strategy: usual care).

[c]Negative costs indicate savings.

[d]Effectiveness expressed as the probability of recurrence of urethral strictures.

[e]Results may appear inexact due to rounding.

[f]Incremental effect = average effect (strategy: DCB) − average effect (strategy: usual care).

[g]Incremental net monetary benefit (INB) was calculated at a WTP of $0 per recurrence using the following formula: incremental effect × WTP – incremental cost. When INB is > 0, the intervention is considered cost-effective and, in this case, cost saving.

One-Way Sensitivity Analyses: Tornado Diagrams

Figures 9 and 10 show 2 tornado diagrams with the results of one-way deterministic analyses for cost and AE parameter input values, respectively. Although changes in the input values resulted in different incremental estimates, paclitaxel-coated balloon dilation remained cost saving when compared with usual care (INB > 0) in all but 1 analysis: when the device cost was at a threshold value of about $4,162 or greater, then paclitaxel-coated balloon dilation would not be cost-saving.

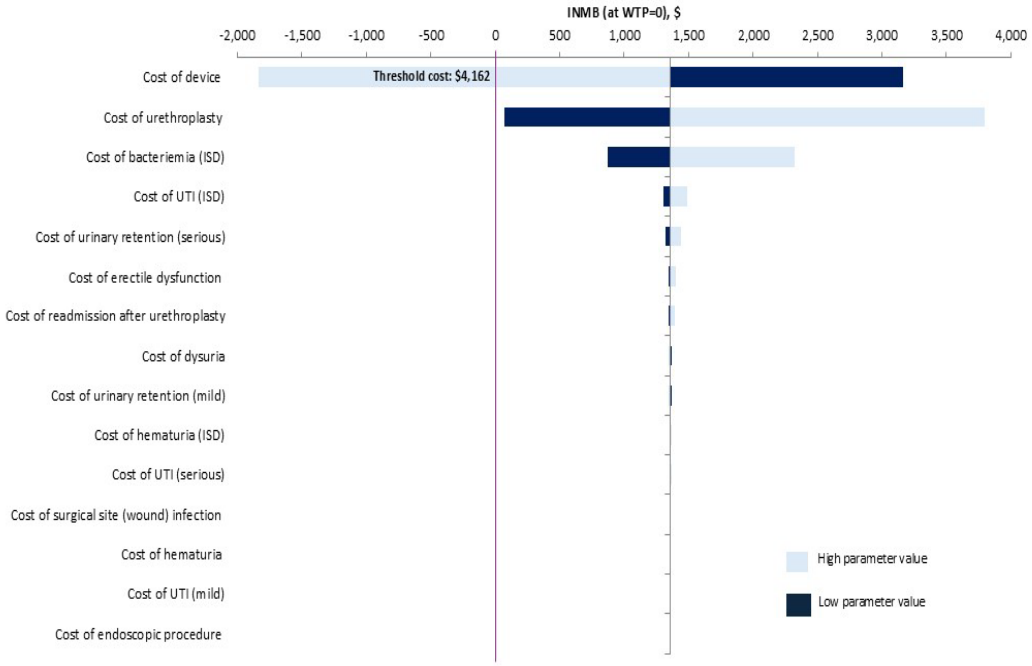

Figure 9: One-Way Analysis Results, Tornado Graph: Uncertainty in Costs

Abbreviations: INMB, incremental net monetary benefit; ISD, intermittent self-dilatation (self-catheterization); UC, usual care; UTI, urinary tract infection; WTP, willingness to pay.

Tornado graph exploring uncertainty in costs using as cost inputs the cost of device, cost of endoscopic procedure, cost of urethroplasty, costs of adverse events such as hematuria, UTI, dysuria, urinary retention (incontinence), bacteriemia, erectile dysfunction, wound infection, or readmission after surgery. The low and high parameter values were presented in the sensitivity analysis. Incremental net monetary benefit in 2025 CAD was calculated at a WTP of $0 per recurrence avoided using the following formula: incremental effect × WTP – incremental cost. When INB is positive or > 0, the intervention is cost saving.

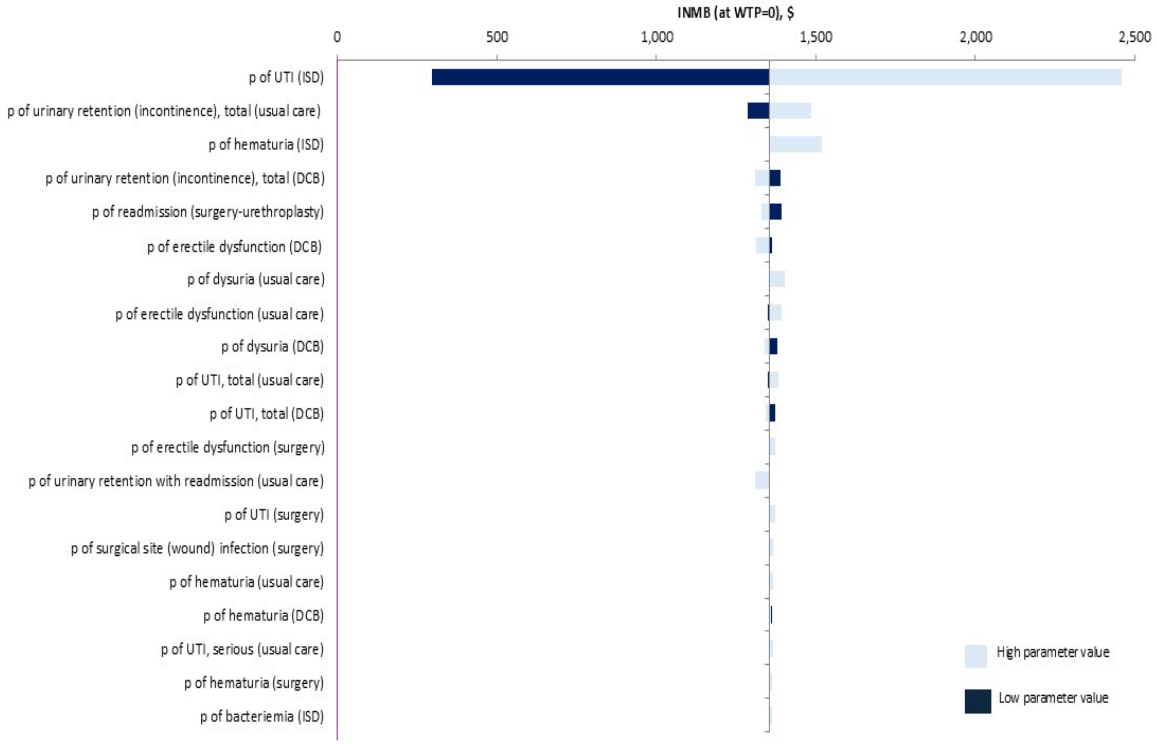

Figure 10: One-Way Analysis Results, Tornado Graph: Uncertainty in Probabilities of Adverse Events

Abbreviations: INMB incremental net monetary benefit; DCB, paclitaxel-coated balloon dilation catheter; ISD, intermittent self-dilatation (self-catheterization); p, probability; UTI, urinary tract infection; WTP, willingness to pay.
Tornado graph exploring the uncertainty in the probability of adverse events. Inputs related to main adverse events following endoscopic, catheterization or surgical procedures include hematuria, UTI, dysuria, urinary retention, bacteriemia, erectile dysfunction, wound infection, and readmission. The low and high parameter values were presented in sensitivity analysis. Incremental net monetary benefit in 2025 CAD was calculated at a WTP of $0 per recurrence avoided using the following formula: incremental effect × WTP – incremental cost. When INB is > 0, then the intervention is cost saving.

Additional Scenarios: Urethroplasty

Table 21 provides the results of the first probabilistic scenario addressing costs and effects of multiple treatment options, including paclitaxel-coated balloon dilation and 2 strategies with urethroplasty. Over the time horizon of 5 years, paclitaxel-coated balloon dilation was the least costly of all options; however, it was also less effective compared with the costlier urethroplasty options (i.e., the surgery done immediately in 75% or 100% of patients reduced overall recurrence by 5% or 23%, respectively).

If WTP was $0 per recurrence avoided, then paclitaxel-coated balloon dilation would be an optimal and cost-saving strategy. However, increasing the WTP to $50,000 per recurrence avoided decreased the

probability of this intervention being cost-effective to 0%. In these scenarios, urethroplasty (in all: 100%) became optimal. In a sequential analysis, 2 strategies were dominated (i.e., excluded because of a lower value) and an ICER of urethroplasty (in all: 100%) versus paclitaxel-coated balloon dilation was estimated at about $24,114 per recurrence avoided.

Table 21: Cost-Effectiveness Scenario – Urethroplasty Compared With Paclitaxel-Coated Balloon Dilation or Usual Care

Strategy[a]	Average total costs, $	Incremental cost, $[a,b,c,d]	Average total effects	Incremental effect,[a,b,c,d]	ICER, $/recurrence avoided, vs. DCB	Probability of strategy being optimal at WTPs of $0, $25,000, $50,000 per recurrence avoided
Paclitaxel-coated balloon dilation	7,189.34		0.51			96.7%, 38.2%, 0%
Usual care	8,665.89	1,476.55	1.71[d]	1.20	Dominated[b]	3.3%, 0%, 0%
Urethroplasty, 75% participation, no wait	10,893.79	3,704.45	0.46	−0.05	74,159.44 Extended dominance[c]	0%, 0%, 0%
Urethroplasty, 100% participation, no wait	12,727.40	5,538.06	0.28	−0.23	24,114.38	0%, 61.8%, 100%

Abbreviations: DCB, paclitaxel-coated balloon dilation; ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.

[a]Treatment strategies are ordered by average total costs, from the lowest to the highest.

[b]"Dominant" indicates the strategy is less costly and more effective than the comparator; "dominated" means that the treatment is more costly and less effective than the comparator.

[c]"Extended dominance" indicates urethroplasty with participation at 75% is ruled out because the ICER for urethroplasty with participation at 75% vs. paclitaxel-coated balloon dilation is higher ($74,159 per recurrence avoided) compared to the ICER for urethroplasty with participation at 100% vs. paclitaxel-coated balloon dilation ($24,114 per recurrence avoided).

[d]All costs in 2025 CAD.

[e]All recurrences counted. In usual care, multiple occurrences were reported, so the number is > 1.

Table 22 provides the results of the second probabilistic scenario analysis that considered upfront treatment with urethroplasty followed by the off-label use of paclitaxel-coated balloon dilation in people who experience recurrence, without or with a possibility of another surgery, after having been previously unsuccessfully treated.

Similar to the previous urethroplasty scenario, paclitaxel-coated balloon dilation done first (i.e., before the urethroplasty) was the least costly of all strategies, but it was also less effective compared with 2 other urethroplasty options (which were associated with a reduction of the recurrence by 16% and 17%). In a sequential analysis, an ICER of the strategy with off-label use of paclitaxel-coated balloon dilation after urethroplasty with the option of a second surgery versus the strategy with paclitaxel-coated balloon dilation done first in all members of the cohort was estimated at about $36,479 per recurrence avoided. This suggests that the off-label use of paclitaxel-coated balloon dilation is cost-effective only if the decision-maker is willing-to-pay an additional $36,479 or more to avoid an additional stricture recurrence in adult males.

Table 22: Cost-Effectiveness Scenario – Off-Label Use of Paclitaxel-Coated Balloon Dilation After Urethroplasty Compared With Paclitaxel-Coated Balloon Dilation or Usual Care

Strategy[a]	Average total costs, $	Incremental cost, $[a,b,c,d]	Average total effects	Incremental effect[a,b,c,d]	ICER, $/recurrence avoided vs. DCB	Probability of strategy being optimal at WTPs of $0; $25,000; $50,000 per recurrence avoided
DCB first	7,189.34		0.51			96.7%, 99.9%, 3.7%
Usual care	8,665.89	1,476.55	1.71[e]	1.20	Dominated[b]	3.3%, 0%, 0%
Off-label DCB use after first urethroplasty, no option for second surgery	13,221.67	6,032.34	0.35	−0.16	38,418.97 Extended dominance[c]	0%, 0%, 0%
Off-label DCB use after first urethroplasty, with an option for second surgery	13,328.36	6,139.02	0.34	−0.17	36,479.02	0%, 0.01%, 96.3%

Abbreviations: DCB, paclitaxel-coated balloon dilation; ICER, incremental cost-effectiveness ratio; WTP, willingness to pay.

[a]Treatment strategies are ordered by average total costs, from the lowest to the highest.

[b]"Dominant" indicates the strategy is less costly and more effective than the comparator; "dominated" means that the treatment is more costly and less effective than the comparator.

[c]"Extended dominance" indicates the strategy is ruled out.

[d]All costs in 2025 CAD.

[e]All recurrences counted. In usual care, multiple occurrences were reported, occurred so the number is > 1.

Discussion

We conducted a primary economic evaluation from the Ministry of Health perspective to determine the cost-effectiveness of paclitaxel-coated balloon dilation compared with usual care for the treatment of recurrent bulbar urethral strictures in adult males in Ontario.

In the reference case, compared with usual care over 5 years, paclitaxel-coated balloon dilation was less costly (−$1,476; 95% CrI: −$3,217 to $112 per person) and more effective with respect to the recurrence reduction of urethral strictures (69%; 95% CrI: 68%–70%). Paclitaxel-coated balloon dilation was cost-effective or cost-saving with a high probability of about 97% or above across a wide range of WTPs.

The cost savings with paclitaxel-coated balloon dilation could be explained mainly by decreases in the need for follow-up procedures, such as a 23.8% reduction of urethroplasty (an invasive surgical option) and a 36.5% reduction in subsequent urethral dilation procedures. Because of the greater effectiveness reported for paclitaxel-coated balloon dilation at the bulbar site (compared to all anterior strictures) over 2 years,[24,25] our scenario analysis showed greater and more likely cost savings with it for the bulbar urethral strictures solely (incremental costs: −$1,824; the probability of the intervention being cost saving: 98%).

Although we found cost savings with paclitaxel-coated balloon dilation (even after using quite conservative assumptions in the costing of this procedure in the reference case analysis), our results remain uncertain and ought to be interpreted with caution. The limitations include the low quality of

currently published clinical evidence that informed our modeling of the effectiveness of paclitaxel-coated balloon dilation. As previously mentioned in the methods section, we rated our certainty in the evidence for the main effectiveness outcomes (based on 1-year data from the ROBUST III RCT and its 2- and 3-year extensions of the paclitaxel-coated balloon catheter arm only[24-26]) according to GRADE as Low to Very low.

Moreover, in their most recent publication on the 3-year-results of the ROBUST III RCT, the authors indicated that "4- and 5-year follow-up data will be critical in determining whether more patients ultimately require retreatment as symptoms or flow rate continue to evolve over time."[26] The long-term (5-year) data are yet to be published at the time of this writing (NCT03499964). Also, there is a prospective, single-arm, open-label, multicenter, observational registry study (NCT05479422) that is evaluating the real-world application of Optilume in patients with recurrent anterior urethral strictures measuring less than 3 cm.

In addition, our scenario analyses showed that these cost-saving results would not have been achieved if we were to assume the following:

- Substantial (2.5×) reduction of the effectiveness of the paclitaxel-coated balloon treatment, resulting in a much higher recurrence rate in the intervention arm and a much smaller recurrence reduction between the strategies (i.e., a difference of < 40% at 5 years), leading to a lack of cost savings (ICER: additional $928 per recurrence avoided)
- Short 1-year time horizon (ICER: $1,796 per recurrence avoided)
- Very long wait time for the urethroplasty (e.g., > 869 days) or a low acceptance or uptake of this surgery (by about 24% of patients), which would result in larger use of urethral dilation or other follow-up procedures in those who fail initial options, and lower use of urethroplasty; in this scenario, favourable effectiveness would not be visible over the 5-year model time horizon
- Larger device costs of more than $4,162 (vs. $2,800 in the reference case)

In addition, our scenarios comparing urethroplasty with paclitaxel-coated balloon dilation (given our reference case assumptions of its effectiveness) suggested the surgery would be a better option if a decision-maker were willing to pay an additional $24,114 to avoid a stricture recurrence in adult males. Similarly, the off-label use of paclitaxel-coated balloon dilation after failing urethroplasty would be considered cost-effective if a decision-maker were willing to pay an additional $36,479 or more to avoid a urethral stricture recurrence in adult males. As mentioned previously, there is no established WTP threshold for those cost-effectiveness analyses assuming a natural effectiveness unit such as the recurrence of urethral strictures, making it difficult to arrive at a valid conclusion on the cost-effectiveness of paclitaxel-coated balloon dilation.

Equity Considerations

Due to limited data, we did not conduct a cost–utility analysis or an equity-related subgroup analysis. We explored the impact of several factors that may affect inequity in access on the reference case results, such as patient acceptance or participation in paclitaxel-coated balloon dilation or in the urethroplasty treatment, age at baseline, cost of follow-up care that needs to be paid by patients out of pocket (e.g., intermittent self-catheterization or indwelling catheters), and the cost of the device.

If paclitaxel-coated balloon dilation is publicly funded in Ontario, more research would be required to describe how different sub-populations might access this new procedure.

In addition, based on expert consultation (W. Shahrour, MD, March 2025; R. Matta, MD, August 25, 2025), there is a concern about the proper use of paclitaxel-coated balloon dilation because the diagnosis and management of bulbar strictures is not always straightforward and requires additional training and resources for urologists, including a fellowship or subspecialty training. These necessary education requirements could pose an additional barrier to access that needs to be examined in future real-world evidence studies.

Strengths and Limitations

Our modelling study provided some new knowledge regarding the short-term benefits and costs of paclitaxel-coated balloon dilation compared with usual care for the treatment of recurrent bulbar urethral strictures in adult males in Ontario. We did not conduct a cost–utility analysis because there was no reliable and valid source for the health utility data associated with the use of this new intervention. It is possible that we would get similar results with the inclusion of the QALY outcome in alignment with potentially high reductions in the recurrence and costs over 5 years, reported in the reference case.

As in any modelling study, our analyses are limited by assumptions related to model structure or to model parameters, but we conducted numerous sensitivity analyses to address or explore these uncertainties. Nevertheless, the quality of the published and evaluated clinical evidence used to inform the modeling of the effectiveness of the intervention versus usual care is low; therefore, our analyses likely overestimated reductions in the stricture recurrence with paclitaxel-coated balloon dilation compared to the reference case. Also, there is no published evidence that directly compared urethroplasty or DVIU with paclitaxel-coated balloon dilation. Because of the limited evidence, we assumed a short time horizon of 5 years, which in turn restricted the modeling, excluding potential long-term benefits and cost-savings that may be achieved with urethroplasty. Our scenario analyses explored conditions under which paclitaxel-coated balloon dilation would not be favourable in terms of the cost-savings or recurrence reduction, and their results could be used to inform and facilitate additional clinical and economic real-world evidence studies in Ontario.

Conclusions

Our economic evaluation found that, compared with usual care, paclitaxel-coated balloon dilation could be less costly and more effective over 5 years for the treatment of recurrent bulbar urethral strictures in adult males in Ontario. Paclitaxel-coated balloon dilation was highly likely cost-effective across a wide range of WTP values in the reference case analysis. However, these results remain uncertain and ought to be interpreted with caution because of the limitations and low quality of the currently published clinical evidence. In scenario analyses, the cost-effectiveness results were sensitive to changes in the effectiveness of the intervention, duration of time horizon, and device cost.

Budget Impact Analysis

Research Question

What is the potential 5-year budget impact for the Ontario Ministry of Health of publicly funding paclitaxel-coated balloon dilation for the treatment of recurrent and symptomatic bulbar urethral strictures in adult males?

Methods

Analytic Framework

We estimated the budget impact of publicly funding paclitaxel-coated balloon dilation for the treatment of recurring bulbar urethral strictures (≤ 3 cm in length) in adult males using the cost difference between 2 scenarios: (1) current clinical practice without public funding for treatment with paclitaxel-coated balloon dilation (the current scenario), and (2) anticipated clinical practice with public funding for treatment with paclitaxel-coated balloon dilation (the new scenario). Figure 11 presents the model schematic.

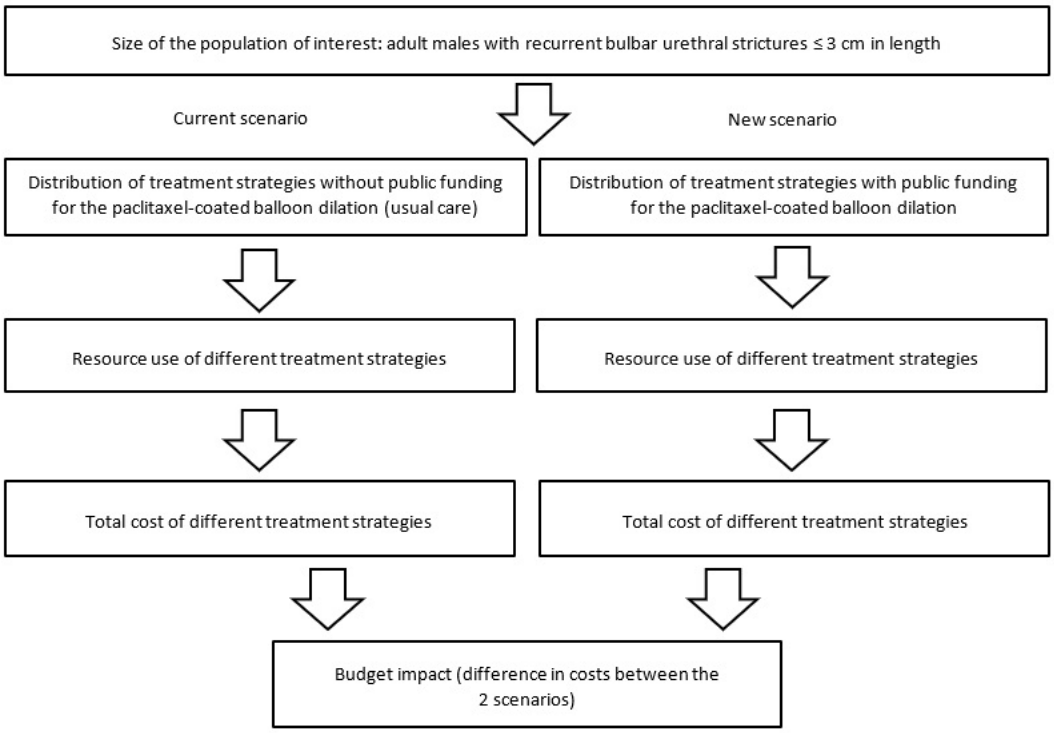

Figure 11: Schematic Model of Budget Impact

Flow chart describing the model for the budget impact analysis. Based on the size of the population of interest, we created 2 scenarios: the current scenario, which would explore the distribution of treatment strategies, resource use, and total costs without public funding for the paclitaxel-coated balloon dilation treatment of recurrent bulbar urethral strictures ≤3 cm in length, and the new scenario, which would explore the distribution of treatment strategies, resource use, and total costs with public funding for paclitaxel-coated balloon dilation. The budget impact would represent the difference in costs between the 2 scenarios.

Key Assumptions

The assumptions used in our primary economic evaluation also apply to the reference case budget impact analysis. In addition, we considered the following:

- Simplifying assumptions used for estimation of the population of interest based on available administrative Ontario data are considered reasonable
- Use of paclitaxel-coated balloon dilation for recurrent bulbar urethral strictures (≤ 3 cm in length) is limited to the scope of sub-specialist urologist care (e.g., reconstructive surgeons; email and oral communications, W. Shahrour, MD, March 2025; R. Matta, MD, March 2 to August 25, 2025)
- Since paclitaxel-coated balloon dilation is not publicly funded (and its current diffusion in Ontario has been relatively small; S. Neu, MD, and R. Matta, MD, oral and email communications, December 13, 2024, to August 25, 2025), zero uptake of this procedure was assumed for the current scenario for Ontario

Population of Interest

Estimate of Population From Procedure Volumes

We approximated the initial size of the population of interest based on administrative data for fiscal years 2018/19 to 2022/23 from the IntelliHealth National Ambulatory Care Reporting System (NACRS) database for Ontario.[56] From this database, we selected data pertinent to adult males (aged ≥ 20 years) treated in the day surgery hospital settings for urethral strictures. Within this cohort, we further estimated annual case volumes of urethral strictures by combining the procedure codes specific to the treatment of urethral strictures (i.e., main treatment procedure as defined by the CCI codes starting with "1PQ50") with relevant main diagnosis disease codes (i.e., ICD-9/ICD-10 codes for unspecified urethral stricture: 598.x/N359).[56]

As shown in Table 23A, the average total volume of urethral dilation or direct vision internal urethrotomy (DVIU) procedures was around 2,115 per year between fiscal years 2018/19 and 2022/23. The smallest number of procedures (N = 1,701) was noted in fiscal year 2020/21, during the COVID-19 pandemic, and the total volume of procedures in the other years ranged from 2,200 to 2,300. Usual care consisted of a variety of urethral dilation procedures, with a flex or rigid dilator (e.g. CCI codes: 1PQ50BABJ, 1PQ50CABJ, 1PQ50BTBP, 1PQ50CABP), laser (e.g., 1PQ50BAAG, 1PQ50CAAG), mechanical balloon (e.g., 1PQ50BABD, 1PQ50CABD), or DVIU (e.g., 1PQ50BA). Excluding the COVID-19 pandemic year, the annual number of procedures using a mechanical balloon ranged from 23 to 43. This corresponded with 1% of the total number of usual care procedures each year. A portion of the mechanical balloon procedures could suggest the use and diffusion of paclitaxel-coated balloon dilation in Ontario (S. Neu, MD, and R. Matta, MD, oral and email communications, December 13, 2024, to March 9, 2025).

From the observed data (excluding the count for the COVID−19 pandemic year of 2020/21), we predicted an overall yearly case volume over the next 5 years using linear extrapolation (Table 23A). The estimated volume of usual care procedures ranged from 2,293 (year 1) to 2,363 (year 5). We considered a mix of urethral dilation and DVIU procedures used for the treatment of urethral strictures in adult males in Ontario.

Table 23A: Case Volume Estimates, Urethral Stricture Dilation/DVIU Procedures Yearly

	2018/19	2019/20	2020/21	2021/22	2022/23	2023/24	Year 1	Year 2	Year 3	Year 4	Year 5
Day surgery (NACRS): number of usual care urethral stricture procedures in adult men											
Observed[a]	2,161	2,204	1,701[a]	2,310	2,195						
Forecast[b]	2,161	2,204	1,701[a]	2,310	2,195	2,166	2,184	2,201	2,219	2,236	2,253
Forecast[c]	2,161	2,204	2,247	2,310	2,195	2,276	**2,293**	**2,310**	**2,328**	**2,345**	**2,363**

Abbreviations: DVIU, direct vision internal urethrotomy; NACRS, the National Ambulatory Care Reporting System.

[a]Observed counts were estimated from the NACRS day surgeries data, filtered on the following variables: adult men (≥ 20 y), main Tx (5 char) CCI codes 1PQ50 (i.e., various types of urethral dilation, including balloon dilation and DVIU) and main diagnosis/disease codes for unspecified urethral strictures (ICD-9 MPDx: 598.x/ ICD-10: N359). The value for the fiscal 2020/21 was lower due to the COVID−19 pandemic.

[b]Forecasted years 1–5 using linear extrapolation from all observed data for the fiscal years 2018/19–2022/23.

[c]Forecasted years 1–5 using linear extrapolation from data for the fiscal years 2018/19–2022/23, excluding the observed COVID-19–related decline in 2020/21 (we imputed 2,247 procedures as an average of the past 2 fiscal years).

Source: Observed data estimated from IntelliHealth Ontario (NACRS day surgeries).[56]

In addition to endoscopic management procedures, and based on expert feedback, we included the number of people currently treated with urethroplasty (where there is a corresponding diagnosis of urethral stricture) for the estimation of the target population because these people could also be treated instead with paclitaxel-coated balloon dilation in the new scenario.

The observed data related to surgical volumes were provided through our collaboration with the Institute for Clinical Evaluative Sciences (ICES) Applied Health Research Question (AHRQ) program (L. Mondor, MSc, N. Troke, MPH, and D. An, MSc, email and oral communications, March to June 24, 2025; see details in Appendix 6). As shown in Table 23B, the average total volume of urethroplasty procedures in Ontario ranged from 168 in 2015/16 to 210 in 2023/24.

Table 23B: Patient Volumes of Urethroplasty Among Adult Men in Ontario by Fiscal Year

	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21	2021/22	2022/23	2023/24
Observed	168	145	184	203	212	152	171	210	210

Source: L. Mondor, MSc, N. Troke, MPH, and D. An, MSc, email and oral communications, March to June 24, 2025.[62] (see Appendix 6 for details).

We used the observed data from Table 23B to estimate annual case volumes for the next 5 years (Table 23C).

Table 23C: Annual Urethroplasty Estimates Used for Estimation of the Population

	Year 1	Year 2	Year 3	Year 4	Year 5
Forecast[a]	208	212	217	222	227

[a]Forecasted using linear extrapolation from the observed data (Table 23B), fiscal years 2015/16–2024/25.

To our predictions of overall procedure case volumes for urethral strictures in Ontario, we applied epidemiologic data to estimate the population of interest (Table 24). Research has found that anterior urethral strictures in adult males represent about 92% of all urethral strictures and, of those, 46.9% are bulbar urethral strictures.[1] Further, the recurrence of urethral strictures in those previously treated with endoscopic usual care procedures (urethral dilation or DVIU) is about 50%.[15] After accounting for these factors, we estimated that between 540 and 559 adult males per year, or a total of about 2,747 adults in Ontario over 5 years, may have recurring bulbar urethral strictures and be potentially eligible for paclitaxel-coated balloon dilation (Table 24).

Table 24: Estimate of Population of Interest: Adult Men With Recurrent Bulbar Urethral Strictures in Ontario

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Adult men treated with DVIU and other dilation procedures (Table 23A)	2,293	2,310	2,328	2,345	2,363	11,639
Adult men treated with urethroplasty (Table 23C)	208	212	217	222	227	1,086
Total number of adult men treated	**2,501**	**2,522**	**2,545**	**2,567**	**2,589**	**12,725**
Adult men treated for anterior urethral strictures (92% of the total)[a]	2,301	2,321	2,341	2,362	2,382	11,707
Adult men with bulbar type of anterior urethral strictures (46.9% of the above)	1,079	1,089	1,098	1,108	1,117	5,491
Adult men with recurrent bulbar urethral strictures (50% of the above)[b]	**540**	**545**	**549**	**554**	**559**	**2,747**

[a]Estimates of adult men with a bulbar type of the male urethral strictures, based on the literature.[1] Calculated as the following example, year 1: 2,501 × 0.92 × 0.469 = 1,079. Some numbers may appear incorrect due to rounding.
[b]Estimates of adult men with recurrent bulbar urethral strictures, assuming a 50% recurrence rate over 1 year.[15] Calculated as the following example, year 1: 2,501 × 0.92 x 0.469 × 0.50 = 540.

Current Intervention Mix

Urethral dilation with the paclitaxel-coated balloon catheter is not publicly funded in Ontario. It is offered at some hospitals in Ontario and is likely covered from hospital global budgets or by hospital research foundations. Some patients pay out of pocket for the paclitaxel-coated balloon catheter (S. Neu, MD, oral communication, December 13, 2024). The most likely procedure codes used for shadow billing urethral dilation procedures with balloon, including the paclitaxel-coated balloon catheter, would be ones that include mechanical balloon for urethral dilation (CCI codes: 1PQ50-BABD or 1PQ50-CABD: "DILATE URETHRA EPO &MECH BALLOON DILAT"; S. Neu, MD, oral communication, December 13, 2024). Based on our assessment of IntelliHealth data (NACRS, day surgery),[56] about 1% to 2% of all eligible procedures shown in Table 23A included the use of a mechanical balloon (23/2,161 in 2018, rising to 40/2,195 in 2022/23). However, we are not clear how many of these procedures could have been using the paclitaxel-coated balloon catheter. Therefore, for simplicity and as the paclitaxel-coated balloon procedures are not publicly funded in Ontario, we assumed that only publicly funded usual care procedures are used in the current scenario for the treatment of recurrent bulbar urethral strictures.

Uptake of the New Intervention and New Intervention Mix

As mentioned (Population of Interest, above, Table 24), using predictions of overall case volumes for urethral strictures in Ontario, between 540 and 559 adult males per year could have recurring bulbar urethral strictures and potentially be eligible for paclitaxel-coated balloon dilation. Due to the limited number of urologists with a subspecialty in reconstructive surgeries, who would be in charge of treating this population in Ontario (R. Matta, MD, personal communication, August 25, 2025), we assumed the following:

- The population of people eligible for paclitaxel-coated balloon dilation would not be expanding over time in the reference case, but uncertainty in the population estimates and uptake were examined in numerous scenarios
- Paclitaxel-coated balloon dilation procedures are used as an alternative treatment option and would substitute or replace the current usual care urethral dilation procedures that were repeatedly used for the treatment of recurrent bulbar urethral strictures

We estimated how quickly the paclitaxel-coated balloon dilation procedure may be adopted with public funding based on our communications with the manufacturer related to market access expansion of this device in past years. Based on this communication, in Canada, the access increased as follows: 15 Optilume devices were sold in 2018, 92 devices in 2019, 185 devices in 2022, 361 devices in 2023, and 566 devices in 2024. Of these, 25% were sold in Ontario (Laborie Medical Technologies, email communication, January 20, 2025).

Based on the rapid increase in the past few years, we assumed that 50% of the eligible population could be treated with paclitaxel-coated balloon dilation in year 1, with uptake rising by 15% in years 2 to 4, reaching 100% in year 5 (Table 25). We tested various uptake rates in the sensitivity analysis.

This uptake rate corresponds to about 2,148 eligible people for paclitaxel-coated balloon dilation over the next 5 years (about 270 in year 1, increasing to 559 in year 5, Table 25). We took a cohort approach to budget impact estimation to account for all treatment costs in this population over 5 years.

Table 25: Uptake of Paclitaxel-Coated Balloon Dilation and Usual Care in Ontario

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
Paclitaxel-coated balloon dilation[a]	—	—	—	—	—	—
Usual care	540	545	549	554	559	2,747
New scenario[b]						
Uptake rate: paclitaxel-coated balloon dilation	50%	65%	80%	95%	100%	—
Paclitaxel-coated balloon dilation	270	354	439	526	559	2,148
Usual care	270	191	110	28	0	599
Total	**540**	**545**	**549**	**554**	**559**	**2,747**

[a]We assumed zero paclitaxel-coated balloon dilation procedures done in the current scenario and no expansion of the patient population over time because of limited human health resources in urology.

[b]We calculated the volume of new interventions with paclitaxel-coated balloon dilation from the total number multiplied by the uptake rate of the intervention (starting at 50% in year 1 and rising by 15% per year in years 2–4, achieving 100% uptake in year 5). For example, in the new scenario, the total volume in year 1 is 540 and the uptake rate is 50%, so the volume of paclitaxel-coated balloon catheter procedures in year 1 is 540 × 50% = 270. Numbers may appear inexact due to rounding.

Resources and Costs

Tables 26 and 27 present the model outputs for yearly cost estimates (total costs and cost broken down by component) for the current scenario with endoscopic management (usual care) and the new scenario with paclitaxel-coated balloon dilation. These cost output estimates (undiscounted costs in 2025 CAD) were generated in the probabilistic model-based analysis (previously described in the primary economic evaluation). They are used in calculations of the total budget impact, taking a cohort-based approach to account for changes in the annual costs over time for each cohort (from year 1 to year 5).

Table 26. Estimated Yearly and Total Costs (Per-Person) Used in the Budget Impact Analysis: Current Scenario (Usual Care Without Paclitaxel-Coated Balloon Dilation)

Current scenario: types of costs	Costs per year and totals (per person), $[a,b]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Endoscopic management: overall procedure cost	1,307.18					1,307.18
Device cost	–	–	–	–	–	–
Reccurence: costs of FU care with urethral dialtion	110.82	378.55	390.44	389.30	388.08	1,657.20
Reccurence: costs of FU care with ISD or indwelling catheter	9.76	33.22	31.91	31.79	31.66	138.35
Urethroplasty	2,309.76	1,146.87	0.19	–	–	3,456.82
Other health care costs	531.65	488.04	420.12	428.73	433.72	2,302.26
Total costs	**4,269.18**	**2,046.68**	**842.67**	**849.82**	**853.46**	**8,861.81**

Abbreviations: FU, follow-up; ISD, intermittent self-catheterization.

[a]All costs in 2025 CAD.

[b]Results may appear inexact due to rounding.

Table 27. Estimated Yearly and Total Costs (Per-Person) Used in Budget Impact Analysis: New Scenario (With Paclitaxel-Coated Balloon Dilation)

New scenario: types of costs	Costs per year and totals (per person), $[a,b]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Endoscopic management: overall DCB procedure cost	4,545.49					4,545.49
Device cost: Optilume[c]	2,800.00	–	–	–	–	–
Reccurence: costs of FU care with urethral dialtion	21.75	75.52	99.91	116.11	118.20	431.49
Reccurence: costs of FU care with ISD or indwelling catheter	1.92	6.63	8.17	9.49	9.65	35.84
Urethroplasty	462.21	310.65	212.04	64.39	3.46	1,052.75
Other health care costs	271.06	228.48	239.29	236.86	233.59	1,209.29
Total costs	**5,302.43**	**621.28**	**559.42**	**426.84**	**364.89**	**7,274.87**

Abbreviations: DCB, paclitaxel-coated balloon dilation; FU, follow-up; ISD, intermittent self-catheterization.

[a]All costs in 2025 CAD.

[b]Results may appear inexact due to rounding.

[c]DCB device costs ($2,800) are included in the overall procedure cost.

Internal Validation

The secondary health economist conducted formal internal validation. This process included testing the mathematical logic of the model, checking for errors, and ensuring the accuracy of parameter inputs and equations.

Analysis

We conducted a model-based reference case analysis and scenario analyses. Our reference case analysis represents the analysis with the most likely set of input parameters and model assumptions. Our sensitivity analyses explored how the results are affected by varying input parameters and model assumptions. All analyses were done from the Ontario Ministry of Health perspective; the patient perspective was considered in a scenario analysis that accounted for the out-off pocket costs for intermittent self-catheterization and indwelling catheters. The budget impact analysis applied the cohort approach over a 5-year time horizon. The budget impact estimates were deterministically calculated using point estimates for the above-presented cost outputs (Tables 26 and 27), in Microsoft Excel for Office 365.[63]

Scenario Analyses

As shown in Table 28, we conducted several scenarios to examine the impact of changes in the uptake, population estimates, costs, and participation in the procedure to see how these factors would impact changes in the net budget impact.

Table 28: Budget Impact Scenario Analyses

Scenarios	Reference Case	Scenarios
Uptake of the paclitaxel-coated balloon dilation procedure	Y1: 50%, Y2–Y4: 15% per year, Y5: 100%	Low: 3% per year, starting from 3% in Y1, rising to 15% in Y5
		Middle and sparse: 10% per year, starting from 10% in Y1, rising to 50% in Y5
		Middle and sparse: 15% per year, starting from 15% in Y1, rising to 75% in Y5
		High and sparse: 20% per year, starting from 20% in Y1, rising to 100% in Y5
Estimate of the population of interest	Table 25	Estimate based on medical services/physician claims data (see Table 30 and Appendix 6)
	Table 25	Smaller: 1/2 × the initial estimate (no change in the uptake)
	Table 25	Higher: 2 x the initial estimate (no change in the uptake)
	Table 25	Higher: 5 × the initial estimate (no change in the uptake)
	Table 25	Extremely high – hypothetical, based on epidemiologic data: see below, Table 31, and Appendix 7: 1,291 in Y1, increasing to 6,779 in Y5, and change in uptake (20% per year)
	Table 24: 92% of the total population (2,301 in Y1)	Assuming 100% of the total number (both anterior and posterior urethra, off-label use; R. Matta, MD, oral and written communication, March 10 and August 25, 2025): e.g., 2,501 in Y1. 2 scenarios: 20% per year uptake and same uptake as in the reference case
Change in the population eligible for urethroplasty	Table 23C (e.g., 208 in Y1)	30% of the current volume specified in Table 24
		70% of the current volume specified in Table 24
Device cost	$2,800	Change in threshold cost ($4,162)
Setting for paclitaxel-coated balloon dilation treatment	Reference case costs: overall procedure (including endoscopy suite) costs: $1,089 and no use of local anesthesia	50/50 ambulatory setting: in 50% of cases, we assumed a smaller procedure cost related to endoscopy suite alone ($459.94, Appendix 4) with the use of local anesthesia, similar to Scenario 12 (Scenarios, Primary Economic Evaluation, above)
Inclusion of out of pocket costs for ISD and indwelling catheter	None, analyses done from the MOH perspective	Inclusion of monthly costs for ISD ($341.21) or indwelling catheters ($10.53), similar to Scenario 10 (see Scenarios, Primary Economic Evaluation, above)
Participation in the initial procedure	100%	75%, similar to the Scenario 4B (see Scenarios, Primary Economic Evaluation, above)

Abbreviations: ISD, intermittent self-catheterization; MOH, Ontario Ministry of Health.

Estimation of Population From Medical Services (OHIP Physician Claims) Data

Appendix 6 provides details on the methods and results of the population estimation for people who had urethral dilation or DVIU procedures from FY 2022/23 to 2023/24, based on the OHIP physician claims data where there was a diagnosis of urethral stricture on record.[62] In brief, the number of adult males (aged ≥ 18 years) who had urethral dilation and DVIU procedures between April 1, 2022 and March 31, 2024 was identified and categorized according to whether they had 1 procedure (i.e.,

1 procedure in the observation period and no procedures in the previous 2 years) or recurrent procedures (i.e., multiple procedures in the observation period or 1 procedure in the observations period and at least 1 procedure in the previous 2 years).

For our estimate of the population of interest in our budget impact, we considered the number of adults with recurrent urethral strictures who were treated repeatedly with endoscopic management procedures in the past 2 years. In the above analysis, there were 1,503 adult males treated for the recurrent disease. As shown in Table 29, we assumed this number for the first year along with a small 3% increase in the population over the remaining years. In addition, we included people treated with urethroplasty (Table 23C) and estimated an overall number of 9,065 adult males potentially treated for urethral stricture disease.

Using the same assumptions to distinguish recurrent urethral bulbar strictures (see Table 24), we estimated a population eligible for treatment with paclitaxel-coated balloon dilation ranging from 738 to 828 per year, or a total of about 3,911 over 5 years (Table 29).

Table 291: Estimate of the Population of Interest From Medical Service (Physician Claims) Data: Adult Men With Recurrent Bulbar Urethral Strictures in Ontario

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Adult men treated urethral strictures[a]	1,503	1,548	1,595	1,642	1,692	7,980
Adult men treated with urethroplasty (Table 23C)	208	212	217	222	227	1,086
Total number of adult men treated for recurrent strictures	**1,711**	**1,760**	**1,812**	**1,864**	**1,918**	**9,065**
Adult men treated for anterior urethral strictures (92% of the total)	1,574	1,619	1,667	1,715	1,765	8,340
Adult men with bulbar type of anterior urethral strictures (46.9% of the above)	**738**	**759**	**782**	**804**	**828**	**3,911**

[a]Estimates assume a 3% per year increase in annual volumes.

Assuming the same uptake as in the reference case, paclitaxel-coated balloon dilation would be used in 3,080 people over the next 5 years (Table 30).

Table 30: Uptake of Paclitaxel-Coated Balloon Dilation and Usual Care in Ontario, Estimate From Medical Service (Physician Claims) Data

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
Paclitaxel-coated balloon dilation[a]	–	–	–	–	–	–
Usual Care	738	759	782	804	828	3,911
New scenario[b]						
Uptake rate: paclitaxel-coated balloon dilation	50%	65%	80%	95%	100%	–
Paclitaxel-coated balloon dilation	369	493	626	764	828	3,080
Usual care	369	266	156	40	0	831
Total	**738**	**759**	**782**	**804**	**828**	**3,911**

[a]We assumed zero paclitaxel-coated balloon dilation procedures done in the current scenario and no expansion of patient population over time because of limited human health resources in urology.

[b]We calculated the volume of new interventions with paclitaxel-coated balloon dilation from the total number multiplied by the uptake rate of the intervention (50% in Year 1, rising by 15% per year in Years 2–4, reaching 100% uptake in Year 5). For example, in the new scenario, the total volume in Year 1 is 738 and the uptake rate is 50%, so the volume of paclitaxel-coated balloon catheter procedures in Year 1 is 738 × 50% = 369. Some numbers may appear inexact due to rounding.

Due to large uncertainty in the population of interest estimates, we conducted another scenario analysis and estimated the population of adult males with all urethral strictures by applying the prevalence data (0.9%) from a US Medicare beneficiary study by Anger et al[64] to the Ontario Ministry of Finance predictions for the Ontario population of males aged 45 years and older over the next 5 years (fiscal years 2025/26 to 2029/30). To estimate the population with recurrent bulbar strictures, we used the same assumptions as previously explained in Table 24, based on the studies by Palminteri et al[1] and Rourke et al.[15] We estimated a population of between 6,454 and 6,779 adult males with recurrent urethral strictures over the next 5 years (Table 31).

We further assumed a 20% per year uptake rate of paclitaxel-coated balloon dilation, leading to about 1,291 adult males being treated with this procedure in Year 1 and a total of about 20,000 over the next 5 years (Appendix 7).

Table 312: Estimate of the Population of Interest From Epidemiologic Data

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Men aged ≥ 45 years, Ontario	3,324,038	3,364,517	3,403,543	3,444,665	3,491,131	17,027,894
Adult men with urethral strictures (0.9% of the above)[64,a]	29,916	30,281	30,632	31,002	31,420	153,251
Adult men with anterior urethral strictures (92% of the above)[1]	27,523	27,859	28,181	28,522	28,906	140,991
Adult men with bulbar urethral strictures (46.9% of the above)[1]	12,908	13,066	13,217	13,377	13,557	66,125
Adult men with recurrent bulbar urethral strictures (50% of the above)[15]	**6,454**	**6,533**	**6,609**	**6,689**	**6,779**	**33,064**

[a]Estimates of urethral strictures in adult men in Ontario based on Ontario population predictions and epidemiologic data.[64] Some numbers may appear inexact due to rounding.

Results

Reference Case

Table 32A presents the overall budget impact of publicly funding paclitaxel-coated balloon dilation in the population of eligible adult males with recurrent bulbar urethral strictures (≤ 3 cm in length). In the current scenario, using endoscopic management procedures, we estimated that total costs range from $2.31 million in year 1 to about $4.91 million in year 5, yielding a total 5-year cost of $18.97 million (treating about 2,747 adult males over 5 years).

Assuming a rapid uptake of the paclitaxel-coated balloon dilation procedure in the new scenario, starting from 50% in year 1, increasing to 100% by year 5, the estimated total costs ranged between $2.58 million and $4.33 million per year over the next 5 years, with a total 5-year cost of $18.22 million (for treating about 2,148 adult males with paclitaxel-coated balloon dilation over 5 years).

The 5-year net budget impact of publicly funding the paclitaxel-coated balloon dilation procedure was cost saving (−$0.74 million), with additional costs of $0.28 million shown for year 1 and annual savings for the remaining years ranging between $0.02 million and $0.58 million.

Table 32A: Budget Impact Analysis Results: Reference Case

Scenario	Annual and total costs and budget impact, $ million[a]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[b]
Current scenario, overall	**2.31**	**3.43**	**3.91**	**4.41**	**4.91**	**18.97**
Usual care	2.31	3.43	3.91	4.41	4.91	18.97
Paclitaxel-coated balloon dilation	–	–	–	–	–	–
New scenario, overall	**2.58**	**3.41**	**3.79**	**4.11**	**4.33**	**18.22**
Usual care	1.15	1.37	1.09	0.73	0.54	4.88
Paclitaxel-coated balloon dilation	1.43	2.05	2.70	3.38	3.79	13.34
Budget impact[b]	**0.28**	**−0.02**	**−0.13**	**−0.30**	**−0.58**	**−0.74**

[a]All costs in 2025 CAD.

[b]Negative costs indicate savings. Results may appear inexact due to rounding. Budget impact calculated as the difference between the total costs in the new and current scenarios.

Table 32B presents the reference case budget impact over the next 5 years by cost component. The highest cost component, associated with additional costs of about $6.96 million over 5 years, was the paclitaxel-coated balloon dilation procedure, including the cost of the device. The estimated cost savings with the new scenario of about $0.74 million over the next 5 years resulted from reductions in downstream treatment costs, for example:

- Reductions in the cost of follow-up care with urethral dilation in people who were not successfully treated with endoscopic management – a 5-year cost savings of about $1.23 million
- Reductions in the imminent need of urethroplasty, yielding cost savings of about $5.03 million over the next 5 years

Table 32B: Budget Impact Analysis Results: Cost Components

Scenario	Annual and total costs and budget impact, $ million[a]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[b,c]
Current scenario	**2.31**	**3.43**	**3.91**	**4.41**	**4.91**	**18.97**
Endoscopic management: overall procedure cost	0.71	0.71	0.72	0.72	0.73	3.59
Device cost: Optilume[d]	0.00	0.00	0.00	0.00	0.00	0.00
Recurrence: costs of FU care with urethral dilation	0.06	0.26	0.48	0.69	0.91	2.40
Recurrence: costs of FU care with ISD or indwelling catheter	0.01	0.02	0.04	0.06	0.08	0.20
Urethroplasty	1.25	1.88	1.89	1.91	1.93	8.85
Other health care costs	0.29	0.55	0.78	1.02	1.27	3.91
New scenario: overall	**2.58**	**3.41**	**3.79**	**4.11**	**4.33**	**18.22**
Endoscopic management: overall paclitaxel-coated balloon dilation procedure cost	1.58	1.86	2.14	2.43	2.54	10.55
Device cost: Optilume[d]	0.76	0.99	1.23	1.47	1.57	6.02
Recurrence: costs of FU care with urethral dilation	0.04	0.15	0.25	0.34	0.40	1.18
Recurrence: costs of FU care with ISD or indwelling catheter	0.00	0.01	0.02	0.03	0.03	0.10
Urethroplasty	0.75	1.00	0.84	0.66	0.57	3.82
Other health care costs	0.22	0.39	0.53	0.66	0.78	2.58
Overall budget impact[b,c,d]	**0.28**	**-0.02**	**-0.13**	**-0.30**	**-0.58**	**-0.74**
Budget impact: overall procedure cost	0.87	1.15	1.42	1.70	1.81	6.96
Budget impact: device cost[d]	0.76	0.99	1.23	1.47	1.57	6.02
Budget impact: costs of FU care with urethral dilation	−0.02	−0.11	−0.22	−0.36	−0.51	−1.23
Budget impact: costs of FU care with ISD or indwelling catheter	0.00	−0.01	−0.02	−0.03	−0.04	−0.10
Budget impact: urethroplasty	−0.50	−0.88	−1.05	−1.25	−1.36	−5.03
Budget impact: other health care costs	−0.07	−0.16	−0.26	−0.37	−0.48	−1.34

Abbreviations: FU, follow-up; ISD, intermittent self-catheterization.

[a]All costs in 2025 CAD.

[b]Negative costs indicate savings.

[c]Results may appear inexact due to rounding.

[d]Device costs included in the overall the paclitaxel-coated balloon dilation procedure cost.

Opportunities for Cost Savings or Health Resource Reduction

As shown above, publicly funding paclitaxel-coated balloon dilation for eligible adult males with recurrent bulbar urethral strictures could result in overall (net) savings over the next 5 years. These net savings result from reductions in downstream costs, such as follow-up monitoring, and procedures, such as continuous use of urethral dilation for the treatment of stricture recurrence or undergoing an invasive surgical procedure (urethroplasty). An increase in the budget in the first year of public funding is mainly related to investing in the cost of the device, which is offset by the potential savings that could occur over the remaining years.

Sensitivity Analysis

Table 33 presents the results of our scenario analyses. While there were changes in the savings with different assumptions of the uptake, population estimates, costs, and participation rates, the cost savings in the new scenario could be highest if:

- The population estimate was more than 2 to 5 times higher than the reference case estimate
- The setting was changed to 50/50 use of local anesthesia and lower costs of endoscopy suites for the paclitaxel-coated balloon procedure
- The costs paid out of pocket by patients for intermittent or indwelling catheters were considered

If the cost of the device were much higher than the reference case cost ($4,162 vs. $2,800), the province would need to pay an additional $2.17 million over 5 years for publicly funding this new procedure.

Table 33: Budget Impact Sensitivity Analysis Results – Scenarios

Scenario	Total 5-year budget impact, $ million[a,b]	Percent change[c]
Reference case (uptake high: Y1: 50%, Y5:100%)	**−0.74**	**NA**
Changes in uptake of paclitaxel-coated balloon dilation compared to reference case		
S1: Uptake of 3% per year	−0.03	−95.35%
S2: Uptake of 10% per year	−0.11	−84.49%
S3: Uptake of 15% per year	−0.17	−76.74%
S4: Uptake of 20% per year (100% in year 5)	−0.23	−69.98%
Estimate of the population of interest		
S5: Based on physician claims (Appendices 6 and 8)	−0.99	33.78%
S6: Smaller: 1/2 × the initial estimate in usual care (540 × 0.5)	−0.37	−49.80%
S7: Higher: 2 × the initial estimate in usual care (540 × 2)	−1.49	100.81%
S8: Higher: 5 × the initial estimate in usual care (540 × 5)	−3.72	402.03%
S9: Extremely high – hypothetical, based on epidemiological data (Appendix 7)	−2.69	263.64%
S10A: 100% of the total number (both anterior and posterior urethra, off-label use (Y1 = 2,501 × 0.50, 20% uptake per year)	−0.53	−28.17%
S10B: 100% of the total number (both anterior and posterior urethra, off-label use (Y1 = 2,501 × 0.50, uptake same as reference case)	−1.72	132.51%
Change in the population eligible for urethroplasty		
S11: 30% of the current volume specified in Table 23C	−0.70	−5.43%
S12: 70% of the current volume specified in Table 23C	−0.72	−2.14%
Device cost		
S13: Change in the device cost ($2,800) to the threshold cost ($4,162)	2.17	−393.64%
Setting for paclitaxel-coated balloon dilation **treatment**		
S14: 50/50 ambulatory setting (50% of the cases: smaller procedure cost with the use of local anesthesia)	−1.57	112.40%
Inclusion of out-of-pocket costs for ISD and indwelling catheter		
S15: Inclusion of monthly costs for ISD ($341.21) or indwelling catheters ($10.53)	−2.06	178.79%
Participation in the initial procedure		
S16: Participation 75%, paclitaxel-coated balloon dilation or usual care (vs. 100% in reference case)	−0.56	−24.70%

Note: Negative numbers indicate cost savings. Negative percentage change suggests decrease in cost savings or additional costs in budget impact scenario compared with the reference case. Positive percentage change suggests an increase in net cost savings in the scenario compared to the reference case.

Abbreviations: ISD, intermittent self-catheterization; NA, not applicable.

[a]All costs in 2025 CAD.

[b]Results may appear inexact due to rounding.

[c]Percentage change calculated as ([the total budget impact of the scenario analysis divided by the total budget impact of the reference case] − 1) × 100.

Discussion

We conducted model-based budget impact analyses to estimate the range of investments needed to publicly fund paclitaxel-coated balloon dilation for eligible adult males with recurrent bulbar urethral strictures in Ontario. This novel procedure was considered not as a first-line treatment option for recurring bulbar strictures but as an option after unsuccessful treatment with usual care (the currently used endoscopic management procedures).

In the reference case, which assumed a high rate of uptake of the procedure, ranging from 50% in year 1 to 100% in year 5, we found cost savings of $0.74 million over the next 5 years. We found an increase in the budget in the first year of public funding due mainly to investing in the cost of the device. These additional costs were balanced with potential savings over the remaining years because of the reductions in the downstream costs, such as follow-up monitoring and procedures such as continuous use of urethral dilation for the treatment of stricture recurrence or undergoing an invasive surgical procedure (e.g., urethroplasty).

The savings in our analyses are highly uncertain and need to be interpreted with caution for the following reasons:

- Unknown effectiveness of paclitaxel-coated balloon dilation versus usual care beyond 5-year time horizon and limitations of the published short-term clinical evidence (i.e., study authors may have overestimated the effectiveness of the intervention because the evidence was derived from data reported for the single paclitaxel-coated balloon arms)
- Uncertainty in the estimate of the population of interest for Ontario
- Uncertainty in the rate of uptake of the intervention

Strengths and Limitations

Our analyses are limited by structural and parameter assumptions and uncertainty in the inputs that informed the modelling. Because of the limitations of both the published short-term literature data used to populate the cost-effectiveness models and the uncertainty in the population estimate, a real-world evidence study for Ontario would be helpful to corroborate the effectiveness and costs of paclitaxel-coated balloon dilation in Ontario.

There is concern about the proper use of paclitaxel-coated balloon dilation because the diagnosis and management of bulbar strictures is not always straightforward and requires additional training and resources of urologists, including a fellowship or subspecialty training (W. Shahrour, MD, email and oral communication, March 2025; R. Matta, MD, email and oral communication, August 25, 2025). This further suggests additional constraints in the capacity of urologists to quickly adopt the intervention, as well as a need for future real-world evidence studies as part of the implementation process that would track and evaluate clinical and cost indicators over time.

Conclusions

Publicly funding paclitaxel-coated balloon dilation in adult males with recurrent bulbar strictures is potentially cost saving, with net savings of about $0.74 million for treating 2,747 adult males over the next 5 years in Ontario. Assuming a high rate of uptake of the procedure (50% in year 1, increasing to 100% in year 5), we found additional costs of $0.28 million in the first year of funding and annual savings for the remaining years (ranging between $0.02 million and $0.58 million per year). These cost-saving estimates ought to be interpreted with caution because our analyses were informed by effectiveness data derived from limited short-term clinical evidence. Future real-world evidence or implementation studies are needed to evaluate the long-term effectiveness and cost-effectiveness of paclitaxel-coated balloon dilation in Ontario.

Preferences and Values Evidence

Objective

The objective of this analysis was to explore the underlying values, needs, and priorities of those who have lived experience with bulbar urethral strictures.

Background

Exploring patient preferences and values provides a unique source of information about people's experiences of a health condition and the health technologies or interventions used to manage or treat that health condition. It includes the impact of the condition and its treatment on the person with the health condition, their family and other care partners, and the person's personal environment. Engagement also provides insights into how a health condition is managed by the province's health system.

Information shared from lived experience can also identify gaps or limitations in published research (e.g., outcomes important to those with lived experience that are not reflected in the literature).[65-67] Additionally, lived experience can provide information and perspectives on the ethical and social values implications of health technologies or interventions.

Because the needs, preferences, priorities, and values of those with lived experience in Ontario are important to consider to understand the impact of a technology or intervention in people's lives, we may speak directly with people who live with a given health condition, including those with experience of the technology or intervention we are exploring.

For this analysis, we examined the preferences and values of people with bulbar urethral strictures who sought or are considering paclitaxel-coated balloon dilation via direct engagement through interviews.

Direct Patient Engagement

Methods

Partnership Plan

The partnership plan for this health technology assessment focused on consultation to examine the experiences of people with bulbar urethral strictures and those of their families and other care partners. We engaged people via phone interviews.

No relevant equity considerations were identified in this health technology assessment; as a result, we did not carry out specific engagement initiatives for distinct populations.

We used a qualitative interview, as this method of engagement allowed us to explore the meaning of central themes in the experiences of people with bulbar urethral strictures, as well as those of their families and care partners.[68] The sensitive nature of exploring people's experiences of a health condition and their quality of life are other factors that support our choice of an interview methodology.

Participant Outreach

We used an approach called purposive sampling,[61,63,69,70] which involves actively reaching out to people with direct experience of the health condition and health technology or intervention being reviewed. We approached clinical experts, support groups, the Ontario Health Patient and Family Engagement Network, and the Ontario Health (Cancer Care Ontario) Patient and Family Advisors to spread the word about this engagement activity and to contact people with bulbar urethral strictures, and their family members and care partners, including those with experience with paclitaxel-coated balloon dilation.

Inclusion Criteria

We sought to speak with adults with bulbar urethral strictures and with care partners. We included those with and without direct experience with paclitaxel-coated balloon dilation.

Exclusion Criteria

We did not set exclusion criteria.

Participants

For this project, we spoke with 4 people with bulbar urethral strictures. Two had direct experience with paclitaxel-coated balloon dilation, 1 of whom resided in and accessed this procedure in another province.

Approach

At the beginning of the interview, we explained the role of our organization, the purpose of this health technology assessment, the risks of participation, and how participants' personal health information would be protected. We gave this information to participants both verbally and in a letter of information (Appendix 9). We then obtained participants' verbal consent before starting the interview. With participants' consent, we audio-recorded and then transcribed the interviews.

Interviews lasted approximately 45 to 60 minutes. The interview was loosely structured and consisted of a series of open-ended questions. Questions were based on a list developed by the Health Technology Assessment International Interest Group on Patient and Citizen Involvement in Health Technology Assessment.[71] Questions focused on the impact of bulbar urethral strictures on the quality of life of people with bulbar urethral strictures, their experiences with treatments to manage or treat bulbar urethral strictures, their experiences with paclitaxel-coated balloon dilation, and their perceptions of the benefits or limitations of paclitaxel-coated balloon dilation. See Appendix 10 for our interview guide.

Data Extraction and Analysis

We used a modified version of a grounded-theory methodology to analyze interview transcripts. The grounded-theory approach allowed us to organize and compare information on experiences across participants. This method consists of a repetitive process of obtaining, documenting, and analyzing responses while simultaneously collecting, analyzing, and comparing information.[72,73] We used the qualitative data analysis software program NVivo[74] to identify and interpret patterns in the data. The patterns we identified allowed us to highlight the impact of bulbar urethral strictures and treatments on the people with bulbar urethral strictures, family members, and care partners we interviewed.

Results

Quality of Life Living With Urethral Strictures

Participants reported that they had been managing urethral strictures for many years, with some people experiencing the condition since adolescence and recurrences throughout their lifetime. Reported causes for their strictures varied, including injury to the area, complications following a prostatectomy, or unknown causes.

> *I first encountered this problem as a young teenager.*
>
> *I don't have any history of traumatic injury to that area, so it's always been a little bit of a mystery.*
>
> *My experience happened after I had a radical prostatectomy.*

The most commonly reported symptom was difficulty fully emptying the bladder, which many described as a constant and frustrating challenge. Other related symptoms included a noticeably reduced urine stream, the need to strain during urination, discomfort while urinating, frequent urination, and recurrent urinary tract infections (UTIs). Due to the recurring nature of this condition, people often required repeated medical interventions and ongoing self-management.

> *I started feeling symptoms of the stricture coming back – a little bit of discomfort when I would go to the bathroom and not completely voiding. I had a couple of instances where I would have a urinary tract infection.*
>
> *I've had difficulty urinating, just either feeling that there was a sense of urgency and then not being able to completely empty.*
>
> *I need to pee very frequently. I mean multiply by 5 or 6 the [number] of times I go to the bathroom compared to someone who doesn't have this problem.*

In more severe instances, participants experienced complete urinary retention, leaving them unable to urinate at all, which led to urgent visits to the emergency department for immediate catheterization. As a result, some participants developed fears about traveling to places that were far from health care facilities.

> *I had to go directly from the airport to an emergency department because I was on a plane and couldn't go, and it's not a pleasant experience.*
>
> *I've had many visits to the emergency department, and they would open it up with a catheter or scope.*
>
> *[I'm] a little bit paranoid to go on trips really far away that would take me outside of the health care system, just in case.*

Participants spoke about the impact of their urethral stricture symptoms on their daily lives. Many found that the unpredictability of their symptoms interfered with multiple areas of their life, including work responsibilities, personal routines, and sleep quality.

> *It doesn't sound like a big deal, but when you put it in the breadth of your entire health and your life and your day-to-day activities, you can see how it bleeds across and effects all the areas and can really screw you up.*

> *Because of the frequent urges to go, you wake up in the night a lot. So, your rest and your sleep is impacted by this problem.*

> *It makes me upset to have to leave a 60-minute meeting midway to use the washroom.*

Many described the constant need to locate nearby bathrooms, which influenced how they planned their day, the routes they took, and whether they felt comfortable leaving home for extended periods.

> *I'm constantly searching where the washrooms are, especially if I'm staying any place for a length of time, just to make sure that when I have that sense of urgency to go I [can] get to the washroom quickly.*

> *I've had to pull over the car to go to the bathroom.*

Participants spoke about the stigma associated with living with urethral stricture. Some mentioned the embarrassment they feel using incontinence products and managing symptoms in public settings, such as having to excuse themselves frequently to find a restroom.

> *I bought the pads myself, which was a bit of an embarrassment.*

> *There's a row of urinals and I'm standing there 3 times [longer than] somebody else; that gets noticed and then you start to get worried about it.*

> *It's more of the embarrassment…maybe I'm avoiding situations and I'm frustrated that I'm not participating as much as I could because that would put me at a distance from a washroom, or [I'd be in a] gathering of people that I didn't know and where I'd have to run off.*

Participants described the mental health impacts of living with urethral strictures. Many explained that the condition was constantly on their minds due to the ongoing risk of recurrences. This worry became particularly heightened during urination, when participants were often unsure whether the experience would be straightforward or accompanied by difficulty, pain, or even a complete blockage. Some participants noted that this unpredictability caused feelings of anxiety and hypervigilance as they found themselves continually anticipating potential complications.

> *I think you worry that, is this going to be the time where I can't go at all? Is the stricture closed up? Am I going to have urinary retention? Am I going to need to be rushed to the hospital? And so, it weighs on you. It's kind of a cumulative*

> *effect of thinking about it all the time and every time that you go to the bathroom with this condition. So, it's very mentally taxing.*
>
> *I would say there's a side effect of a lot of anxiety that builds around it because of what it is. You're always aware of this issue. You're always aware when you need to use the bathroom. You are always worried about the problem worsening, because that's the nature of it.*

Care Journey to Manage Urethral Strictures

Participants spoke about their care journey to manage urethral strictures, which were recurrent from the time of their initial diagnosis. They described the ongoing and often frustrating cycle of symptoms returning even after receiving treatment, which prompted them to continuously explore treatment options in hopes of preventing a recurrence. Over the years, participants reported undergoing multiple procedures, including direct vision internal urethrotomy (DVIU), cystoscopies, and self-dilation. Treatments may have offered temporary or long-term relief, but often led to a recurrence of the stricture.

> *In 15 years, I have had 3 cystoscopies where the stricture has been. They've tried to correct it, but eventually scar tissue grows back.*
>
> *When I had my first stricture, it was about every 2 years I was having a procedure done. Since the last one, it's been almost 6 [years].*
>
> *I was originally operated on with the DVIU procedure…. I would say that that procedure lasted for the better part of 10 or more years. [After that,] I had a cystoscopy done and there was evidence of a stricture at the time, but the doctor said it's kind of up to me whether I want to have it operated on again.*

Participants discussed the recovery process following the different treatment options they underwent, many of which required catheterization. Several described this aspect of recovery as particularly difficult, noting that catheterization was often painful and uncomfortable.

> *For me, personally, just having had the 3 stricture procedures, the part that absolutely terrifies me is the catheter at the end. I had contractions, and I was spasming on it, and the last one I took out myself.*
>
> *I was also provided with catheters so I could self-catheterize. I would [have to] just open it up and go, which was not pleasant.*

In some cases, participants reported delaying treatment for their urethral stricture due to fear or stigma associated with the condition. Fear was often linked to concerns about the invasiveness of procedures and the potential for pain or discomfort during or after the treatment. Stigma contributed to delays, as participants felt embarrassed about their condition and were hesitant to seek medical attention.

> *I'll just live with it a while longer because even getting it treated, it's kind of scary and uncomfortable and even a little painful. And so, I think that's a barrier for some men.*

> *I'm pretty open with my health care provider, but it took me a while to go in and see him. The embarrassment kind of slowed me down in seeking treatment.*

Paclitaxel-Coated Balloon Dilation

All participants highlighted the importance of relying on their health care providers for guidance when deciding on the most suitable treatment for their urethral stricture. They valued the expertise and knowledge of their providers and described decision-making as a collaborative effort.

> *I think it's imperative that your provider, whether it's a urologist or a cardiologist, whoever gives you all the options, that you trust what they're telling you and that they have your best interests at heart. I believe wholeheartedly that my urologist does. We've had that kind of relationship.*

> *I know these guys who do it are very, very trained and skilled, so I will be deferring a lot to the experts.*

> *My doctor explained to me that I basically had 3 options. One was to do another DVIU. The second was to do Optilume.… And then the third one would be to go for the more invasive urethroplasty.*

Recurrence rates were an important factor in participants' decision-making when choosing a treatment option for urethral stricture. They described weighing the benefits and drawbacks of different treatment approaches based on how likely the stricture was to return. While most participants preferred paclitaxel-coated balloon dilation because of its minimally invasive nature, some did state that it was challenging to choose between a more invasive procedure such as urethroplasty that might provide longer-lasting results versus a less invasive procedure that could have a shorter recurrence-free period.

> *The DVIU recurrence rates are very high, relative to some other procedures. I didn't feel at the time that it was really worth going through it again.*

> *With Optilume, we discussed it with my doctor. You know that the data is obviously more limited, but pretty good success rates at 3 and 5 years from the initial studies that have been done.*

> *The other part that stopped me was that it's [Optilume] not a cure, it's more of an ongoing treatment and it may have to be repeated. So that made me stop and think, well, is this worth it?*

Participants expressed hesitancy towards a more invasive treatment option, such as urethroplasty, even though this procedures offered the potential benefit of reduced recurrence of urethral strictures. Their reluctance was largely tied to concerns about the invasiveness and recovery process, particularly given the sensitivity of the area being treated and the potential for pain, discomfort, and complications. As a result, many participants stated a preference for minimally invasive procedures, which they perceived as less burdensome and easier to recover from, even if they carried a higher risk of recurrence.

> *It would be preferable to the other [more] invasive procedures. If it can be done minimally invasive, it is better for everybody. You know the patient has less hospital stay, less chance of other types of problems or infections [than from a more] invasive procedure.*

> *With urethroplasty, I still felt that was too much to go through. I've got a young family. I've got a pretty demanding job. And so, the recovery time associated with that procedure just felt like it's very much a last resort for me.*

> *I find that it's a really intimidating surgery when they explain it to you.*

When asked about the potential short-term impact of paclitaxel on fertility, participants said it was not a concern for them at their current stage of life. However, they noted it would be a concern if they were planning to have children in the future.

> *I think that that ship has sailed. But if I were 29 or 39, I think that would be something you would want to consider for sure.*

> *That was not a concern for me because our family is complete. But as I understand it, Optilume has minimal risk in relation to both fertility and erectile dysfunction.*

Two participants had undergone paclitaxel-coated balloon dilation. One was a month post-procedure, while the other had it over a year ago. Both describe the procedure as fairly straightforward and they did not require an overnight hospital stay. There were differences in experiences for anesthesia use, where 1 participant was fully sedated while the other was given regional anesthesia during the procedure. The person receiving regional anesthesia described the procedure as uncomfortable. The settings differed as well, with 1 being performed in a hospital setting in Ontario while the other took place in a private clinic in another province.

> *I was put under fully, so general anesthetic. It was day surgery, so I was in and out.*

> *The Optilume procedure was booked and completed in his office as an outpatient procedure. It was about 45 minutes from start to finish…, so I was awake the whole time. It's not comfortable, even with the [inhaled pain reliever]. You do feel things. I wouldn't describe it as being overly painful. But I would describe it as being quite uncomfortable. Yeah, it's not pleasant.*

The people who underwent paclitaxel-coated balloon dilation spoke about their recovery experience, which consisted of having a catheter at home for a few days – which required them to miss work. The recovery process also required follow-up appointments for monitoring.

> *I went back home with a catheter the same day and had it removed 2 days later in his [doctor's] office. Then it was just post-operative care… I have a follow up scheduled about a month from the procedure. At that time, we'll do a urine flow test.*

> *I was home 4 to 5 days with a catheter in place. I came back at the 3-month mark for a cystoscopy, and then I was due to come back for a 1-year cystoscopy.*

One participant described a painful recovery process after the paclitaxel-coated balloon dilation procedure, noting that they experienced substantial pain when urinating during the recovery period. They also expressed frustration from not having been informed beforehand about the amount of pain possible during recovery.

> *That pain was pretty pronounced. It kind of feels like you've got shards of glass in that area of the body when you're going to the bathroom…. It's normal to feel discomfort, but nobody prepared me for the type of pain…like I said that that pain did go away.*

People we spoke with who had direct experience of paclitaxel-coated balloon dilation reported being able to fully empty their bladder after the initial recovery period following the procedure. They also reported improvements in other related symptoms, including improved urine stream and improved mental health.

> *I'm going to the bathroom more easily. My stream is strong, I feel good. I'm glad I had it done. It's been positive and I'm really glad I got it done. I'm peeing well, I feel good. I don't worry about getting a UTI. I feel like I have voided completely – there's nothing being held back when I'm finished.*

> *After the procedure last year, I felt great. I was functioning very well. [The doctor said] "We can pass the scope all the way through into your bladder. That's really, really good. You're obviously functioning very well."*

One participant reported experiencing a recurrence of the urethral stricture after the procedure. This caused disappointment, but they noted their symptoms are more manageable than prior to undergoing paclitaxel-coated balloon dilation.

> *I went back for my follow up, and [the doctor said], "We see the beginning of the structures recurred." Right now, post-Optilume, I'm doing better than I was before. Some of the symptoms I'm talking about aren't as intense as they were, say, 5 or 6 years ago. Unfortunately, in my case, the structure has recurred…. I am without question managing better even with the recurrence, having had the Optilume versus not. It was disappointing, but it wasn't a shock. I was aware of the statistics.*

In this case, the participant noted that even though paclitaxel-coated balloon dilation had not worked for them, it helped reduce their hesitancy to undergo urethroplasty, which is a more invasive procedure. This feeling was echoed by another participant, who stated that urethroplasty was a last resort.

> *I'm still scared of the bigger surgery [urethroplasty], but I'm more resolved that it's the right thing to do now.*

> *I can always do urethroplasty at a later date if this [Optilume] fails…. It's very much a last resort for me.*

Barriers to Accessing Paclitaxel-Coated Balloon Dilation

A majority of participants were not aware of paclitaxel-coated balloon dilation as a treatment option for urethral strictures. Of the 2 who had undergone the procedure, 1 became aware of it through their care provider and the other through online research.

> *I became aware of it when I was finally seen by a reconstructive urologist. He then explained to me that this was a possible treatment option. I had no idea it existed before that.*

Cost was another notable barrier. Paclitaxel-coated balloon dilation is available in a limited number of private clinics, with patients paying out of pocket for the procedure. It is publicly funded in only a few hospitals across Ontario. One participant who underwent the procedure privately described feeling fortunate to have the financial means to do so.

> *All in, it was probably around $7000, from start to finish…. We're on 1 salary, and we did get some help from both of our parents…to cover some of the cost…. I was fortunate to be able to pay for it.*

Geography was also mentioned as a barrier to accessing paclitaxel-coated balloon dilation due to it being available through public funding in a limited number of hospitals. Those who underwent paclitaxel-coated balloon dilation expressed gratitude for being able to access the procedure. One participant waited until paclitaxel-coated balloon dilation was offered near them.

> *I think the geographic thing is huge, living in the GTA [greater Toronto area], …I think it's only 1 hospital that does Optilume in the GTA, it didn't matter to me which hospital I was initially sent to because I knew I could find my way there somehow.*

> *I knew it existed and I had really just been kind of wondering and waiting when I could find a doctor near me who offered it.*

Some participants described challenges in accessing health care providers who specialize in urethral strictures. This was particularly difficult in smaller cities, where specialists were limited, and when trying to see a reconstructive urologist with specific expertise in urethral strictures rather than a general urologist.

> *My urologist has also just retired, so I don't have a follow up. They don't tend to replace specialists as they leave, it's hard to attract them to the area.*

> *My experience with a regular urologist versus a reconstructive urologist – it's very clear that the latter knows so much more about strictures. It really wasn't until I got in front of a reconstructive urologist that I felt that they really knew how to deal with this issue.*

Discussion

Direct engagement with people with lived experience of urethral strictures allowed us to gather perspectives and examine their preferences and values, the factors that influenced their decision-making regarding treatment, and the impact of paclitaxel-coated balloon dilation on their health and quality of life. All participants shared their experiences with living with urethral strictures and its impact on all aspects of their daily lives, as well as the mental health effects of having dealt with the recurrent nature of the condition. They shared their treatment journey, undergoing repeated procedures, as well as the burden of the recovery process and their hesitancy around undergoing urethroplasty. Paclitaxel-coated balloon dilation was seen as a good option due to it being a minimally invasive treatment for urethral strictures.

One limitation of our review was the limited number of people we were able to speak with who have lived experience with urethral strictures. We attribute this limitation to the stigma surrounding the condition. Additionally, we have low representation from people who have undergone paclitaxel-coated balloon dilation, which was likely due to the procedure currently being publicly funded in only a limited number of hospitals across Ontario, as well as lack of awareness of the procedure among people with urethral strictures. We had limited perspectives from rural communities and no representation from Northern Ontario. Another limitation is that the participants who had undergone urethral stricture had the procedure between a month and about a year before we spoke to them, so the long-term impact of the treatment remains unclear.

Conclusions

Paclitaxel-coated balloon dilation was viewed favourably by all those we interviewed, especially given the hesitancy by participants to undergo urethroplasty. Those with experience of paclitaxel-coated balloon dilation reported a reduction in their symptoms related to urethral strictures, including the ability to fully empty their bladder. Though 1 participant who underwent the procedure experienced a recurrence, they noted that it helped them come to terms with undergoing the more invasive procedure (urethroplasty). This increased openness to urethroplasty if the paclitaxel-coated balloon procedure fails was echoed by the other participant who had undergone the procedure. Those who had not undergone paclitaxel-coated balloon dilation mentioned being open to the procedure due to it being a minimally invasive treatment option.

Barriers to accessing paclitaxel-coated balloon dilation included lack of awareness of the procedure, the out-of-pocket cost when accessing it through a private clinic, and geography (because the procedure is available in only a limited number of publicly funded hospitals). Participants emphasized that implementation should include more equitable access.

Conclusions of the Health Technology Assessment

There is currently no evidence for a head-to-head comparison between paclitaxel-coated balloon dilation and direct vision internal urethrotomy – the most common treatment method for bulbar urethral stricture in Ontario. While freedom from reintervention favoured the intervention group, this may have been overestimated due to censoring "informative" participants (GRADE: Low). This treatment may improve urinary symptoms and urine flow rate (GRADE: Low). The rate of hematuria and dysuria during the first month after treatment was higher in the intervention group than in the control group (GRADE: Moderate).

Paclitaxel-coated balloon dilation may be more effective and less costly than usual care for adult males with unsuccessfully treated recurrent and symptomatic bulbar urethral strictures. Publicly funding paclitaxel-coated balloon dilation in this population is potentially cost saving, with the net savings of about $0.74 million from treating 2,747 adult males over the next 5 years in Ontario. Assuming a high rate of uptake of the procedure (50% in year 1, increasing to 100% in year 5), additional costs of $0.28 million are expected in the first year of funding, and annual savings for the remaining years (ranging between $0.02 million and $0.58 million per year). These cost-savings estimates ought to be interpreted with caution because our analyses were informed by the effectiveness data derived from limited and low-quality clinical evidence (GRADE: Low; risk of bias: high).

People with bulbar urethral strictures with whom we spoke reported hesitancy about undergoing urethroplasty and viewed paclitaxel-coated balloon dilation favourably because it is a minimally invasive procedure. Barriers to access included lack of awareness of the procedure, the out-of-pocket cost when accessing it through a private clinic, and distance from hospitals or clinics performing the procedure.

Abbreviations

CI: confidence interval

CPI: consumer price index

CrI: credible interval

DVIU: direct vision internal urethrotomy

EAC: External Assessment Center

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

HTA: health technology assessment

ICER: incremental cost-effectiveness ratio

ICES: Institute for Clinical Evaluative Sciences

IIEF: international index of erectile function

INB/INMB: incremental net monetary benefit

IPSS: international prostate symptom score

MTAC: Medical Technologies Advisory Committee

NACRS: National Ambulatory Care Reporting System

NHS: National Health Services

NICE: National Institute for Health and Care Excellence

OHIP: Ontario Health Insurance Plan

PCB: paclitaxel-coated balloon

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PSS: Personal Social Services

PVR: post-void residual volume

QALY: quality-adjusted life year

Qmax: maximum flow rate

QOL: quality of life

RCT: randomized controlled trial

SD: standard deviation

UTI: urinary tract infection

WTP: willingness to pay

Glossary

Adverse event: An adverse event is an unexpected medical problem that happens during treatment for a health condition. Adverse events may be caused by something other than the treatment.

Base case: In economic evaluations, the base case is the "best guess" scenario, including any assumptions, considered most likely to be accurate. In health technology assessments conducted by Ontario Health, the reference case is used as the base case.

Budget impact analysis: A budget impact analysis estimates the financial impact of adopting a new health care intervention on the current budget (i.e., the affordability of the new intervention). It is based on predictions of how changes in the intervention mix will impact the level of health care spending for a specific population. Budget impact analyses are typically conducted for a short-term period (e.g., 5 years). The budget impact, sometimes referred to as the net budget impact, is the estimated cost difference between the current scenario (i.e., the anticipated amount of spending for a specific population without using the new intervention) and the new scenario (i.e., the anticipated amount of spending for a specific population following the introduction of the new intervention).

Cohort model: In economic evaluations, a cohort model is used to simulate what happens to a homogeneous cohort (group) of patients after receiving a specific health care intervention. The proportion of the cohort who experiences certain health outcomes or events is estimated, along with the relevant costs and benefits. In contrast, a microsimulation model follows the course of individual patients.

Cost–consequence analysis: A cost–consequence analysis is a type of economic evaluation that estimates the costs and consequences (i.e., the health outcomes) of two or more health care interventions. In this type of analysis, the costs are presented separately from the consequences.

Cost-effective: A health care intervention is considered cost-effective when it provides additional benefits, compared with relevant alternatives, at an additional cost that is acceptable to a decision-maker based on the maximum willingness-to-pay value.

Cost-effectiveness acceptability curve: In economic evaluations, a cost-effectiveness acceptability curve is a graphical representation of the results of a probabilistic analysis. It illustrates the probability of health care interventions being cost-effective over a range of willingness-to-pay values. Willingness-to-pay values are plotted on the horizontal axis of the graph, and the probability of the intervention of interest and its comparator(s) being cost-effective at corresponding willingness-to-pay values is plotted on the vertical axis.

Cost-effectiveness analysis: Used broadly, "cost-effectiveness analysis" may refer to an economic evaluation used to compare the benefits of two or more health care interventions with their costs. It may encompass several types of analysis (e.g., cost-effectiveness analysis, cost–utility analysis). Used more specifically, "cost-effectiveness analysis" may refer to a type of economic evaluation in which the main outcome measure is the incremental cost per natural unit of health (e.g., life-year, symptom-free day) gained.

Cost-effectiveness plane: In economic evaluations, a cost-effectiveness plane is a graph used to show the differences in cost and effectiveness between a health care intervention and its comparator(s).

Differences in effects are plotted on the horizontal axis, and differences in costs are plotted on the vertical axis.

Cost-minimization analysis: In economic evaluations, a cost-minimization analysis compares the costs of two or more health care interventions. It is used when the intervention of interest and its relevant alternative(s) are determined to be equally effective.

Cost–utility analysis: A cost–utility analysis is a type of economic evaluation used to compare the benefits of two or more health care interventions with their costs. The benefits are measured using quality-adjusted life-years, which capture both the quality and quantity of life. In a cost–utility analysis, the main outcome measure is the incremental cost per quality-adjusted life-year gained.

Decision tree: A decision tree is a type of economic model used to assess the costs and benefits of two or more alternative health care interventions. Each intervention may be associated with different outcomes, which are represented by distinct branches in the tree. Each outcome may have a different probability of occurring and may lead to different costs and benefits.

Deterministic sensitivity analysis: Deterministic sensitivity analysis is an approach used to explore uncertainty in the results of an economic evaluation by varying parameter values to observe the potential impact on the cost-effectiveness of the health care intervention of interest. One-way sensitivity analysis accounts for uncertainty in parameter values one at a time, whereas multiway sensitivity analysis accounts for uncertainty in a combination of parameter values simultaneously.

Discounting: Discounting is a method used in economic evaluations to adjust for the differential timing of the costs incurred and the benefits generated by a health care intervention over time. Discounting reflects the concept of positive time preference, whereby future costs and benefits are reduced to reflect their present value. The health technology assessments conducted by Ontario Health use an annual discount rate of 1.5% for both future costs and future benefits.

Disease-specific preference-based measures: Disease-specific preference-based measures are instruments used to obtain the quality-adjusted weight (i.e., the utility value) of being in a particular health state or having a specific health condition. Disease-specific preference-based measures are often thought to be more sensitive than generic preference-based measures in capturing condition-specific health effects. Like generic preference-based measures, disease-specific preference-based measures typically consist of a self-completed questionnaire, a health-state classification system, and a scoring formula that calculates the utility value. The key difference is that health states in disease-specific preference-based measures are important for the health condition of interest but may not apply to all patient populations. Examples of disease-specific preference-based measures include the Diabetes Utility Index (DUI) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

Dominant: A health care intervention is considered dominant when it is more effective and less costly than its comparator(s).

EQ-5D: The EQ-5D is a generic health-related quality-of-life classification system widely used in clinical studies. In economic evaluations, it is used as an indirect method of obtaining health state preferences (i.e., utility values). The EQ-5D questionnaire consists of five questions relating to different domains of quality of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each domain, there are three response options: no problems, some problems, or severe problems. A newer

instrument, the EQ-5D-5L, includes five response options for each domain. A scoring table is used to convert EQ-5D scores to utility values.

Equity: Unlike the notion of equality, equity is not about treating everyone the same way.[16] It denotes fairness and justice in process and in results. Equitable outcomes often require differential treatment and resource redistribution to achieve a level playing field among all individuals and communities. This requires recognizing and addressing barriers to opportunities for all to thrive in our society.

Extended dominance: A health care intervention is considered to be extendedly dominated when it has an incremental cost-effectiveness ratio higher than that of the next most costly or effective comparator. Interventions that are extendedly dominated are ruled out.

Generic preference-based measures: Generic preference-based measures are generic (i.e., not disease specific) instruments used to obtain the quality-adjusted weight (i.e., the utility value) of being in a given health state. Generic preference-based measures typically consist of a self-completed questionnaire, a health-state classification system, and a scoring formula that calculates the utility value. Examples include the Health Utilities Index Mark 3 (HUI3), the EQ-5D, and the Short Form–Six Dimensions (SF-6D). The quality-adjusted weights are obtained from the public or from patients, who are provided with a descriptive profile of each predefined health state and asked to fill out a questionnaire. The benefit of using a generic instrument is the ability to obtain utility values that are comparable across different health care interventions and diseases.

Health inequity: Health inequities are avoidable inequalities in health between groups of people within countries and between countries.[75] These inequities arise from inequalities within and between societies. Social and economic conditions and their effects on people's lives determine their risk of illness and the actions taken to prevent them becoming ill or treat illness when it occurs.

Health-related quality of life: Health-related quality of life is a measure of the impact of a health care intervention on a person's health. It includes the dimensions of physiology, function, social life, cognition, emotions, sleep and rest, energy and vitality, health perception, and general life satisfaction.

Health state: A health state is a particular status of health (e.g., sick, well, dead). A health state is associated with some amount of benefit and may be associated with specific costs. Benefit is captured through individual or societal preferences for the time spent in each health state and is expressed in quality-adjusted weights called utility values. In a Markov model, a finite number of mutually exclusive health states are used to represent discrete states of health.

Incremental cost: The incremental cost is the additional cost, typically per person, of a health care intervention versus a comparator.

Incremental cost-effectiveness ratio (ICER): The incremental cost-effectiveness ratio (ICER) is a summary measure that indicates, for a given health care intervention, how much more a health care consumer must pay to get an additional unit of benefit relative to an alternative intervention. It is obtained by dividing the incremental cost by the incremental effectiveness. Incremental cost-effectiveness ratios are typically presented as the cost per life-year gained or the cost per quality-adjusted life-year gained.

Incremental net benefit: Incremental net benefit is a summary measure of cost-effectiveness. It incorporates the differences in cost and effect between two health care interventions and the

willingness-to-pay value. Net health benefit is calculated as the difference in effect minus the difference in cost divided by the willingness-to-pay value. Net monetary benefit is calculated as the willingness-to-pay value multiplied by the difference in effect minus the difference in cost. An intervention can be considered cost-effective if either the net health or net monetary benefit is greater than zero.

Markov model: A Markov model is a type of decision-analytic model used in economic evaluations to estimate the costs and health outcomes (e.g., quality-adjusted life-years gained) associated with using a particular health care intervention. Markov models are useful for clinical problems that involve events of interest that may recur over time (e.g., stroke). A Markov model consists of mutually exclusive, exhaustive health states. Patients remain in a given health state for a certain period of time before moving to another health state based on transition probabilities. The health states and events modelled may be associated with specific costs and health outcomes.

Ministry of Health perspective: The perspective adopted in economic evaluations determines the types of costs and health benefits to include. Ontario Health develops health technology assessment reports from the perspective of the Ontario Ministry of Health. This perspective includes all costs and health benefits attributable to the Ministry of Health, such as treatment costs (e.g., drugs, administration, monitoring, hospital stays) and costs associated with managing adverse events caused by treatments. This perspective does not include out-of-pocket costs incurred by patients related to obtaining care (e.g., transportation) or loss of productivity (e.g., absenteeism).

Monte Carlo simulation: Monte Carlo simulation is an economic modelling method that derives parameter values from distributions rather than fixed values. The model is run several times, and in each iteration, parameter values are drawn from specified distributions. This method is used in microsimulation models and probabilistic analysis.

Multiway sensitivity analysis: A multiway sensitivity analysis is used to explore uncertainty in the results of an economic evaluation. It is done by varying a combination of model input (i.e., parameter) values simultaneously between plausible extremes to observe the potential impact on the cost-effectiveness of the health care intervention of interest.

Natural history of a disease: The natural history of a disease is the progression of a disease over time in the absence of any health care intervention.

One-way sensitivity analysis: A one-way sensitivity analysis is used to explore uncertainty in the results of an economic evaluation. It is done by varying one model input (i.e., a parameter) at a time between its minimum and maximum values to observe the potential impact on the cost-effectiveness of the health care intervention of interest.

Probabilistic analysis: A probabilistic analysis (also known as a probabilistic sensitivity analysis) is used in economic models to explore uncertainty in several parameters simultaneously and is done using Monte Carlo simulation. Model inputs are defined as a distribution of possible values. In each iteration, model inputs are obtained by randomly sampling from each distribution, and a single estimate of cost and effectiveness is generated. This process is repeated many times (e.g., 10,000 times) to estimate the number of times (i.e., the probability) that the health care intervention of interest is cost-effective.

Quality-adjusted life-year (QALY): The quality-adjusted life-year (QALY) is a generic health outcome measure commonly used in cost–utility analyses to reflect the quantity and quality of life-years lived. The life-years lived are adjusted for quality of life using individual or societal preferences (i.e., utility

values) for being in a particular health state. One year of perfect health is represented by one quality-adjusted life-year.

Reference case: The reference case is a preferred set of methods and principles that provide the guidelines for economic evaluations. Its purpose is to standardize the approach of conducting and reporting economic evaluations, so that results can be compared across studies.

Scenario analysis: A scenario analysis is used to explore uncertainty in the results of an economic evaluation. It is done by observing the potential impact of different scenarios on the cost-effectiveness of a health care intervention. Scenario analyses involve varying structural assumptions from the reference case.

Sensitivity analysis: Every economic evaluation contains some degree of uncertainty, and results can vary depending on the values taken by key parameters and the assumptions made. Sensitivity analysis allows these factors to be varied and shows the impact of these variations on the results of the evaluation. There are various types of sensitivity analysis, including deterministic, probabilistic, and scenario.

Societal perspective: The perspective adopted in an economic evaluation determines the types of costs and health benefits to include. The societal perspective reflects the broader economy and is the aggregation of all perspectives (e.g., health care payer and patient perspectives). It considers the full effect of a health condition on society, including all costs (regardless of who pays) and all benefits (regardless of who benefits).

Time horizon: In economic evaluations, the time horizon is the time frame over which costs and benefits are examined and calculated. The relevant time horizon is chosen based on the nature of the disease and health care intervention being assessed, as well as the purpose of the analysis. For instance, a lifetime horizon would be chosen to capture the long-term health and cost consequences over a patient's lifetime.

Tornado diagram: In economic evaluations, a tornado diagram is used to determine which model parameters have the greatest influence on results. Tornado diagrams present the results of multiple one-way sensitivity analyses in a single graph.

Uptake rate: In instances where two technologies are being compared, the uptake rate is the rate at which a new technology is adopted. When a new technology is adopted, it may be used in addition to an existing technology, or it may replace an existing technology.

Utility: A utility is a value that represents a person's preference for various health states. Typically, utility values are anchored at 0 (death) and 1 (perfect health). In some scoring systems, a negative utility value indicates a state of health valued as being worse than death. Utility values can be aggregated over time to derive quality-adjusted life-years, a common outcome measure in economic evaluations.

Willingness-to-pay value: A willingness-to-pay value is the monetary value a health care consumer is willing to pay for added health benefits. When conducting a cost–utility analysis, the willingness-to-pay value represents the cost a consumer is willing to pay for an additional quality-adjusted life-year. If the incremental cost-effectiveness ratio is less than the willingness-to-pay value, the health care intervention of interest is considered cost-effective. If the incremental cost-effectiveness ratio is more than the willingness-to-pay value, the intervention is considered not to be cost-effective.

Appendices

Appendix 1: Literature Search Strategies

Clinical Evidence Search

Search Date: June 6, 2024

Databases searched: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and NHS Economic Evaluation Database

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <May 2024>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to June 5, 2024>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2024 Week 22>, Ovid MEDLINE(R) ALL <1946 to June 05, 2024>
Search Strategy:
---
1 Urethral Stricture/ (10987)
2 (urethr* adj3 (narrow* or stenos#s or stricture* or widen*)).ti,ab,kf. (18217)
3 or/1-2 (22029)
4 Coated Materials, Biocompatible/ (19234)
5 (drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*) adj5 balloon*).ti,ab,kf. (8550)
6 (balloon* adj5 drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).ti,ab,kf. (8479)
7 (DEB or DEBs or DCB or DCBs).ti,ab,kf. (13196)
8 exp Paclitaxel/ (178568)
9 ((paclitax* or ptx or abraxane* or anzatax* or onxol* or paxene* or praxel* or taxol*) adj5 (balloon* or catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).ti,ab,kf,nm. (16244)
10 (PEB or PEBs or PCB or PCBs).ti,ab,kf,nm. (47450)
11 optilum*.ti,ab,kf. (133)
12 or/4-11 (259460)
13 3 and 12 (144)
14 exp Animals/ not Humans/ (16526203)
15 13 not 14 (128)
16 (Comment or Editorial or (Letter not (Letter and Randomized Controlled Trial)) or Conference Proceeding or Congress).pt. (4658741)
17 15 not 16 (105)
18 limit 17 to english language [Limit not valid in CDSR; records were retained] (104)
19 18 use medall,coch,cctr,cleed (28)
20 urethra stenosis/ (6608)
21 (urethr* adj3 (narrow* or stenos#s or stricture* or widen*)).tw,kw,kf. (18398)
22 or/20-21 (20615)
23 drug-coated balloon/ (3012)
24 drug-eluting balloon catheter/ (143)

25 (drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*) adj5 balloon*).tw,kw,kf,dv. (8685)
26 (balloon* adj5 drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).tw,kw,kf,dv. (8616)
27 (DEB or DEBs or DCB or DCBs).tw,kw,kf,dv. (13290)
28 paclitaxel coated balloon catheter/ (384)
29 ((paclitax* or ptx or abraxane* or anzatax* or onxol* or paxene* or praxel* or taxol*) adj5 (balloon* or catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).tw,kw,kf,dv,du,dy,tn. (16402)
30 (PEB or PEBs or PCB or PCBs).tw,kw,kf,dv. (47485)
31 optilum*.tw,kw,kf,tn,dv. (144)
32 or/23-31 (78818)
33 22 and 32 (118)
34 (exp animal/ or nonhuman/) not exp human/ (12156132)
35 33 not 34 (106)
36 Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (9481147)
37 35 not 36 (53)
38 37 use emez (15)
39 19 or 38 (43)
40 39 use medall (19)
41 39 use emez (15)
42 39 use coch (0)
43 39 use cctr (9)
44 39 use cleed (0)

Economic Evidence Search

Search Date: September 23, 2024

Databases searched: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and NHS Economic Evaluation Database

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <August 2024>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to September 18, 2024>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2024 Week 38>, Ovid MEDLINE(R) ALL <1946 to September 19, 2024>
Search Strategy:
---
1 Urethral Stricture/ (11168)
2 (urethr* adj3 (narrow* or stenos#s or stricture* or widen*)).ti,ab,kf. (18427)
3 or/1-2 (22300)
4 Coated Materials, Biocompatible/ (19576)
5 (drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*) adj5 balloon*).ti,ab,kf. (8888)
6 (balloon* adj5 drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).ti,ab,kf. (8815)
7 (DEB or DEBs or DCB or DCBs).ti,ab,kf. (13605)

8 exp Paclitaxel/ (181476)
9 ((paclitax* or ptx or abraxane* or anzatax* or onxol* or paxene* or praxel* or taxol*) adj5 (balloon* or catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).ti,ab,kf,nm. (16463)
10 (PEB or PEBs or PCB or PCBs).ti,ab,kf,nm. (47943)
11 optilum*.ti,ab,kf. (145)
12 or/4-11 (263637)
13 3 and 12 (153)
14 exp Animals/ not Humans/ (16610380)
15 13 not 14 (137)
16 limit 15 to english language [Limit not valid in CDSR; records were retained] (136)
17 16 use coch,cleed (0)
18 economics/ (266567)
19 economics, medical/ or economics, pharmaceutical/ or exp economics, hospital/ or economics, nursing/ or economics, dental/ (1119422)
20 economics.fs. (477173)
21 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).ti,ab,kf. (1396010)
22 exp "costs and cost analysis"/ (720817)
23 (cost or costs or costing or costly).ti. (353377)
24 cost effective*.ti,ab,kf. (497904)
25 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kf. (334643)
26 models, economic/ (16803)
27 markov chains/ or monte carlo method/ (114917)
28 (decision adj1 (tree* or analy* or model*)).ti,ab,kf. (75789)
29 (markov or markow or monte carlo).ti,ab,kf. (193066)
30 quality-adjusted life years/ (60771)
31 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).ti,ab,kf. (123682)
32 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).ti,ab,kf. (223228)
33 or/18-32 (3642263)
34 16 and 33 (4)
35 34 use medall,cctr (3)
36 17 or 35 (3)
37 urethra stenosis/ (6760)
38 (urethr* adj3 (narrow* or stenos#s or stricture* or widen*)).tw,kw,kf. (18610)
39 or/37-38 (20884)
40 drug-coated balloon/ (3196)
41 drug-eluting balloon catheter/ (148)
42 (drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*) adj5 balloon*).tw,kw,kf,dv. (9026)
43 (balloon* adj5 drug* adj5 (catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).tw,kw,kf,dv. (8955)
44 (DEB or DEBs or DCB or DCBs).tw,kw,kf,dv. (13699)
45 paclitaxel coated balloon catheter/ (431)
46 ((paclitax* or ptx or abraxane* or anzatax* or onxol* or paxene* or praxel* or taxol*) adj5 (balloon* or catheter* or coat* or deliver* or device* or dilat* or elut* or emitt* or releas*)).tw,kw,kf,dv,du,dy,tn. (16638)
47 (PEB or PEBs or PCB or PCBs).tw,kw,kf,dv. (47981)

48 optilum*.tw,kw,kf,tn,dv. (157)
49 or/40-48 (80082)
50 39 and 49 (126)
51 (exp animal/ or nonhuman/) not exp human/ (12272129)
52 50 not 51 (114)
53 limit 52 to english language [Limit not valid in CDSR; records were retained] (114)
54 Economics/ (266567)
55 Health Economics/ or Pharmacoeconomics/ or Drug Cost/ or Drug Formulary/ (156667)
56 Economic Aspect/ or exp Economic Evaluation/ (582820)
57 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw,kw,kf. (1416656)
58 exp "Cost"/ (720817)
59 (cost or costs or costing or costly).ti. (353377)
60 cost effective*.tw,kw,kf. (506886)
61 (cost* adj2 (util* or efficac* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kw,kf. (345082)
62 Monte Carlo Method/ (88827)
63 (decision adj1 (tree* or analy* or model*)).tw,kw,kf. (79238)
64 (markov or markow or monte carlo).tw,kw,kf. (196560)
65 Quality-Adjusted Life Years/ (60771)
66 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw,kw,kf. (127054)
67 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw,kw,kf. (244333)
68 or/54-67 (3137853)
69 53 and 68 (13)
70 69 use emez (1)
71 36 or 70 (4)
72 71 use medall (3)
73 71 use emez (1)
74 71 use coch (0)
75 71 use cctr (0)
76 71 use cleed (0)
77 remove duplicates from 71 (4)

Grey Literature Search

Performed on: June 18-21, 2024

Websites searched:

Alberta Health Evidence Reviews, BC Health Technology Assessments, Canada's Drug Agency (CDA-AMC), Institut national d'excellence en santé et en services sociaux (INESSS), Institute of Health Economics (IHE), University Of Calgary Health Technology Assessment Unit, Ontario Health Technology Assessment Committee (OHTAC), McGill University Health Centre Health Technology Assessment Unit, Centre Hospitalier de l'Universite de Quebec-Universite Laval, Contextualized Health Research Synthesis Program of Newfoundland (CHRSP), Health Canada Medical Device Database, International HTA Database (INAHTA), Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers, Centers for Medicare & Medicaid Services Technology Assessments, Veterans Affairs Health Services Research and Development, Institute for Clinical and Economic Review, Oregon Health

Authority Health Evidence Review Commission, Washington State Health Care Authority Health Technology Reviews, National Institute for Health and Care Excellence (NICE), National Health Service England (NHS), Healthcare Improvement Scotland, Health Technology Wales, Ireland Health Information and Quality Authority Health Technology Assessments, Adelaide Health Technology Assessment, Australian Government Medical Services Advisory Committee, Monash Health Centre for Clinical Effectiveness, The Sax Institute, Australian Government Department of Health and Aged Care, Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), Pharmac, Italian National Agency for Regional Health Services (Aegnas), Belgian Health Care Knowledge Centre, Ludwig Boltzmann Institute for Health Technology Assessment (Austria), The Regional Health Technology Assessment Centre (HTA-centrum), Swedish Agency for Health Technology Assessment and Assessment of Social Services, Norwegian Institute of Public Health - Health Technology Assessments, The Danish Health Technology Council, Ministry of Health Malaysia - Health Technology Assessment Section, Tuft's Cost-Effectiveness Analysis Registry, PROSPERO, EUnetHTA,ClinicalTrials.gov

Keywords used: urethra, urethral, stenosis, stricture, balloon, catheter, optilume, paclitaxel

Clinical results (included in PRISMA): 2
Economic results (included in PRISMA): 2
Ongoing HTAs (PROSPERO/EUnetHTA/NICE/MSAC): 3
Ongoing clinical trials: 9

Appendix 2: Critical Appraisal of Clinical Evidence

Table A1: Risk of Bias[a] in the ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: Repeat Intervention

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al, 2022[24]	Some concerns[b]	High[c]	Low	Some concerns[d]	Low	High

Abbreviation: DVIU, direct vision internal urethrotomy.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

[c]In the intervention group, the stricture was predilated before the treatment. Patients were not blinded to the treatment after 6 months.

[d]The decision to proceed with repeat intervention was at the discretion of the surgeon performing test for urethral lumen patency.

Table A2: Risk of Bias[a] in the ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: Anatomical Success

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al, 2022[24]	Some concerns[b]	High[c]	Low	Some concerns[d]	Low	High

Abbreviation: DVIU, direct vision internal urethrotomy.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

[c]In the intervention group, the stricture was predilated before the treatment. The test was not performed for all patients and the study added participants who had repeat intervention to those who failed the test.

[d]The decision to proceed with repeat intervention was at the discretion of the surgeon performing test for urethral lumen patency.

Table A3: Risk of Bias[a] for ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: Qmax and PVR

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al, 2022[24]	Some concerns[b]	High[c]	Low	Low	Low	High

Abbreviations: DVIU, direct vision internal urethrotomy; PVR, postvoid residual urine volume; Qmax, maximum flow rate.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

[c]In the intervention group, the stricture was predilated before the treatment. Patients were not blinded to the treatment after 6 months.

Table A4: Risk of Bias[a] for the ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: IPSS and IPSS – QOL

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al, 2022[24]	Some concerns[b]	High[c]	Low	Low	Low	High

Abbreviations: DVIU, direct vision internal urethrotomy; IPSS, international prostate symptom scores; QOL, quality of life.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

[c]In the intervention group, the stricture was predilated before the treatment. Patients were not blinded to the treatment after 6 months.

Table A5: Risk of Bias[a] for the ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: Sexual Function

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al, 2022[24]	Some concerns[b]	Low	Low	Low	Low	Low

Abbreviation: DVIU, direct vision internal urethrotomy.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

Table A6: Risk of Bias[a] for the ROBUST III Trial for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture: Adverse Events

Author, year	Bias due to randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias due to selection of the reported results	Overall risk of bias
Elliott et al 2022[24]	Some concerns[b]	Low	Low	Low	Low	Low

Abbreviation: DVIU, direct vision internal urethrotomy.

[a]Possible risk of bias levels: low, high, some concerns. Risk of bias assessed using RoB 2.[21]

[b]No information on allocation concealment.

Table A7: Risk of Bias[a] for the ROBUST III Trial for Pharmacodynamic Assessments in 15 Non-randomized Participants[b]

Criteria for determining risk of bias	Result
Clear criteria for inclusion	Not clear
Condition measured in standard way for all participants	Not clear
Use of a valid method for identification of condition	Not clear
Consecutive inclusion of participants	Not clear
Clear reporting of participants' demographics	Not clear
Clear reporting of participants' information	Not clear
Clear reporting of outcomes and follow-ups	Not clear
Clear reporting of the site demographic information	Not clear
Use of appropriate statistical analysis	Not clear

[a]Through JBI critical appraisal checklist for case series.
[b]Elliott et al, 2022.[24]

Table A8: GRADE Evidence Profile for the Comparison of Paclitaxel-Coated Balloon Dilation and Other Endoscopic Treatments in Patients With Bulbar Urethral Stricture

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Repeat intervention							
1 (RCT)	Serious limitations (–1)[a]	Serious limitations (–1)[b]	Serious limitations (–1)[c]	No serious limitations	Undetected	None	⨁⨁ Low
Anatomical success							
1 (RCT)	Serious limitations (–1)[a]	Serious limitations (–1)[b]	Serious limitations (–1)[c]	No serious limitations	Undetected	None	⨁ Very low
Functional outcomes (Qmax, PVR)							
1 (RCT)	Serious limitations (–1)[a]	Serious limitations (–1)[b]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
IPSS, IPSS-QOL							
1 (RCT)	Serious limitations (–1)[a]	Serious limitations (–1)[b]	No serious limitations	No serious limitations	Undetected	None	⨁⨁ Low
Sexual function							
1 (RCT)	No serious limitations	Serious limitations (–1)[b]	No serious limitations	No serious limitations	Undetected	None	⨁⨁⨁ Moderate
Adverse events							
1 (RCT)	No serious limitations	Serious limitations (–1)[b]	No serious limitations	No serious limitations	Undetected	None	⨁⨁⨁ Moderate
Systemic exposure to paclitaxel and concentration of paclitaxel in semen							
1 (Case series, n = 15)	Serious limitations (–2)[c]	Serious limitations (–1)[b]	Undetected	Undetected	Undetected	None	⨁ Very low
Effect of paclitaxel on quality of semen, infertility, damage to germ cells, teratogenicity							

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
No study							Cannot be assessed

Notes for Table A8

Abbreviations: DVIU, direct vision internal urethrotomy; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IPSS, international prostate symptom score; PVR, postvoid residual volume; Qmax, maximum value of the urine flow rate measured in mL/s; QOL, quality of life; RCT, randomized controlled trial.

[a]Due to high in risk of bias.

[b]Variation in point estimates due to between-study differences cannot be determined when only 1 study is available.

[c]Lack of clinical applicability and generalizability.

[c]Due to high risk of bias assessed by JBI tool.

Appendix 3: Results of Applicability and Limitation Checklists for Studies Included in the Economic Literature Review

Table A9: Assessment of the Applicability of Economic Studies Evaluating Paclitaxel-Coated Balloon Dilation

Author, year, country	Is the study population appropriate for the review question?	Are the interventions appropriate for the review question?	Is the system in which the study was conducted sufficiently like the current Ontario context?	Is the perspective of the costs appropriate for the review question (e.g., Canadian public payer)?	Is the perspective of the outcomes appropriate for the review question?	Are all future costs and outcomes discounted appropriately (as per current CDA guidelines)?	Are QALYs derived using CDA's preferred methods, or is an appropriate social care–related equivalent used as an outcome? (If not, describe rationale and outcomes used in line with the analytical perspective taken)	Overall judgment[a]
NICE, 2022,[33] United Kingdom	Yes	Intervention with Optilume (paclitaxel-coated balloon dilation): appropriate comparator	Partially	Partially, NHS, and PSS	Unclear	Partially, base case: 3.5% Additional analyses: 2% and 4%	NA	Partially applicable
Kelly, 2023,[34] United Kingdom (submitted to MTAC-NICE)	Yes	Intervention with Optilume (paclitaxel-coated balloon dilation): appropriate comparator	Partially	Partially, NHS, and PSS	Unclear	Partially, base case: 3.5% Additional analyses: 2% and 4%	NA	Partially applicable

Note: Response options for all items were "yes," "partially," "no," "unclear," and "NA" (not applicable).

Abbreviations: CDA, Canada's Drug Agency; MTAC, Medical Technologies Advisory Committee; NA, not applicable; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PPS, Personal Social Services; QALY, quality-adjusted life-year.

[a]Overall judgment may be "directly applicable," "partially applicable," or "not applicable."

Table A10: Assessment of the Limitations of Economic Studies Evaluating Paclitaxel-Coated Balloon Dilation

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputsa match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
NICE, 2022,[33] United Kingdom	Partially: repeated or second use of Optilume (paclitaxel-coated balloon dilation) may not be appropriate in Ontario	Yes	Partially: CUA not perfomed due to no assessment of the QALY outcome	Partially: no long-term RCT data to support evaluation of multiple use of Optilume (paclitaxel-coated balloon dilation) for reccurent urethral strictures	Yes	Yes	Yes	Yes	Partially: cost consequence analysis	Yes	NA/Unclear: NICE assessemnt of manufacturer's submission	Potentially serous limitaions
Kelly, 2023,[34] United Kingdom (submitted to MTAC-NICE)	Partially	Yes	Partially	Partially	Yes	Yes	Yes	Yes	Partially	Yes	NA/Unclear	Potentially serous limitaions

Note: Response options for all items were “yes,” “partially,” “no,” “unclear,” and “NA” (not applicable).

Abbreviations: CUA, cost-utility analysis; MTAC, Medical Technologies Advisory Committee; NA, not applicable; NICE; National Institute for Health and Care Excellence; QALY, quality-adjusted life-year; RCT, randomized controlled trial.

[a]Clinical inputs include relative treatment effects, natural history, and utilities.

[b]Overall judgment may be “minor limitations,” “potentially serious limitations,” or “very serious limitations.”

Appendix 4: Estimate of Usual Care Procedure Costs

Table A11: Estimate of Usual Care Day Surgery Procedure Costs, Per-Person

Usual care endoscopic day surgery procedures for male urethral strictures[a,b]	Average (min; max)
All eligible day-surgery procedures (2022/23)	$1,089.58 ($16.20; $5,446.26)
Eligible day-surgery procedures that are not endoscopy (2022/23)	$1,380.18 ($16.20; $5,446.26)
Eligible day-surgery procedures, endoscopy (2022/23)	$459.94 ($63.99; $2,324.98)

Abbreviation: NACRS, National Ambulatory Care Reporting System.

[a]Overall volume of eligible day surgery procedures for 2022/23: 2,195. Number of endoscopy procedures: 1,130 (about 51%).

[b]NACRS data combined on the following variables: day surgery, male, age ≥ 20 y (311 of 2,195 patients, LT 45 y), ICD9 MPDx Code (4 char): 598.x (MPDx: N359), CCI procedure (Main Tx [5 char] Code): 1PQ50. About 51% of all day surgery procedures were done as day surgery endoscopy.

Source: NACRS, IntelliHealth.[56]

Table A12: Estimate of Urethroplasty (Inpatient) Procedure Costs, Per-Person

	FY: 2022/23, number of people discharged (%)[a]	Total cost[a]				LOS, days[a]			
		Mean	STD	Min	Max	Mean	STD	Min	Max
Age: 18–69 y	104 (87%)	$9,710	$19,204	$2,478	$202,078	1.4	0.6	1	4
Age: ≥ 70 y	16 (13%)	$7,981	$3,976	$4,137	$18,210	1.3	0.7	1	3
Overall (weighted estimates)	**120 (100%)**	**$9,479.67**	**$17,173.91**	**$2,699.27**	**$177,562.08**	**1.37**	**0.61**	**1.00**	**3.87**

Abbreviations: DAD, Discharge Abstract Database; FY, fiscal year; LOS, length of stay; STD, standard deviation.

[a]DAD, FY: 2022/23, variables: 1) Principal procedure: Urethroplasty (CCI codes: (1PQ80BA) REPAIR URETHRA EPO & SIMPL APPOS, (1PQ80BAW0) REPAIR URETHRA EPO &OTH SYNTHETIC, (1PQ80BAXXA) REPAIR URETHRA EPO & AUTOGR, (1PQ80HAW0) REPAIR URETHRA PERC APP &OTH SYNTHETIC, (1PQ80LA) REPAIR URETHRA OA, (1PQ80LAAD) REPAIR URETHRA OA &CRYOPROB, (1PQ80LAXXA) REPAIR URETHRA OA & AUTOGR, (1PQ80LAXXE) REPAIR URETHRA OA& LOC FLP, (1PQ80LAXXG) REPAIR URETHRA OA & PED FLP, (1PQ80LAXXQ) REPAIR URETHRA OA & COMBO TIS); 2) Most responsible diagnosis block: (N30-N39) OTHER DISEASES OF URINARY SYSTEM; 3) Most responsible diagnosis: (N350) POST-TRAUMATIC URETHRAL STRICTURE, (N351) POSTINFECTIVE URETHRAL STRICTURE, NOT ELSEWHERE CLASSIFIED, (N358) OTHER URETHRAL STRICTURE, (N359) URETHRAL STRICTURE, UNSPECIFIED.

Source: Case Costing Analysis Tool - Acute Inpatients, IntelliHealth.[56]

Appendix 5: Reference Case Analysis Results, Undiscounted Effectiveness Outcome

Table A13: Reference Case Analysis Results: Cost-Effectiveness Outcomes (Undiscounted and Discounted Effectiveness Outcomes)

Strategy	Total costs‡ Mean (95% CrI)	Incremental cost[a,b,c‡] Mean (95% CrI)	Total effects, recurrence[c,d,e] Mean (95% CrI)	Incremental effect[c,d,e] Mean (95% CrI)	ICER[c,f]
			0.9981 (0.9980; 0.9982)†		
Usual care	$8,665.91 ($7,315.49; $10,793.27)‡		0.9882 (0.9879; 0.9885)‡		
			0.3041 (0.2957; 0.3126)†	−0.6940 (−0.7024; −0.6855) †	
Paclitaxel-coated balloon dilation	$7,189.47 ($6,072.26; $8,507.80)‡	−$1,476.44 (−$3,217.15; $112.40)‡	0.2984 (0.2901; 0.3069)‡	−0.6898 (−0.6980; −0.6813)‡	**Dominant:** more effective and less costly

Abbreviations: CrI, credible interval; ICER, incremental cost-effectiveness ratio.

[a]Incremental cost = average cost (paclitaxel-coated balloon dilation) − average cost (usual care). All costs are expressed in 2025 CAD, the discount rate of 1.5%‡.

[b]Negative costs indicate savings.

[c]Results may appear inexact due to rounding.

[d]Incremental effect = average effect (paclitaxel-coated balloon dilation) − average effect (usual care). The effectiveness outcome was defined as recurrence after initial endoscopic management (i.e., reintervention needed at 5 years, as determined by the clinical outcome: freedom from reintervention).

[e]Two estimates for the effectiveness outcome were presented: one undiscounted† and another discounted‡ (rate: 1.5%).

[f]The incremental cost-effectiveness ratio was calculated by dividing the mean incremental cost with the mean incremental effect. It is expressed as additional $ gained or averted per additional unit of effect.

Appendix 6: Health Technology Assessment to Evaluate Urethral Drug-Coated Balloon (Optilume) for Recurrent Bulbar Urethral Strictures in Adult Men, Applied Health Research Question (AHRQ): TRIM# 2026 0950 196 000

Acknowledgement & Disclaimers[62]

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These datasets were linked using unique encoded identifiers and analyzed at ICES.

Methods and Results

Methods and results provided in the section below.

Study Period
Study population 1 (usual care): April 1, 2022 to March 31, 2024 (FYs 2022/23 and 2023/24). **Study population 2 (urethroplasty):** April 1, 2015 to March 31, 2024 (FYs 2015/16 to 2023/24).

Study Population
Study population 1 (usual care): Adult men (age ≥ 18 y) who had urethral dilation or direct visual internal urethrotomy (DVIU) procedures from FY 2022/23 to 2023/24. **Study population 2 (urethroplasty):** Adult men (age ≥ 18 y) who had urethroplasty procedures in each FY from 2015/16 to 2023/24. These study populations align with the needs of the health technology assessment being conducted by Ontario Health. Each population was derived independently.

Inclusion / Exclusion Criteria
Cohort inclusion criteria
From the OHIP physician claims data, we identified all records of urethral dilation and DVIU procedures among adult men (study population 1) and urethroplasty procedures each year among adult men (study population 2), where there was a diagnosis of urethral stricture on the same claims record. The codes used to identify the study populations are listed in the Appendix 1 worksheet. The OHIP physician claims data was used to facilitate the capture of events taking place in physician offices (i.e., urologist's office). The OHIP fee codes for urethral dilation and DVIU (as well as

urethroplasty) used in this AHRQ project have been previously used by urologists/clinical experts who work with ICES data.

Cohort exclusion criteria (applied to each study population)

1. Invalid ICES Key Number (IKN)
2. Records with data quality issues – date of birth coded after the OHIP service date, date of death coded prior to the OHIP service date, sex missing in the RPDB
3. Non-Ontario residents at OHIP service date
4. OHIP ineligible at OHIP service date
5. Aged < 18 y at OHIP service date

Analysis

We identified the number of adult men who had a urethral dilation or a DVIU procedure from April 1, 2022 to March 31, 2024. We described the characteristics of patients in terms of their age, Ontario Health region of residence, area-level income quintile (quintile 5 represents the highest income areas of the province), and material resources quintile (quintile 5 represents the most marginalized areas of the province in terms of material resources) according to whether the patient had 1 procedure (i.e., 1 procedure in the observation period and no procedures in the prior 2 years) or recurrent procedures (i.e., multiple procedures in the observation period or 1 procedure in the observations period and at least 1 procedure in the prior 2 years). The target population included patients with recurrent procedures.

We then identified the number of patients undergoing urethroplasty procedures annually (i.e., by fiscal year) from April 1, 2015 to March 31, 2024. The number of patients was ascertained overall each year and further by age, Ontario Health region, income quintile, and material resources quintile.

Limitations

We did not quantify select adverse events among the target population (including hematuria, dysuria, urinary tract infection, urinary retention, and erectile dysfunction) due to concerns of under-capture in health administrative data records for the population of interest.

We were unable to quantify health care costs specific to urethral dilation, DVIU, and urethroplasty procedures among the target population. ICES maintains a costing methodology that allocates the total provincial health care operational budget financed by the Ontario Ministry of Health to provincial residents at each instance of health care use. This enables enumeration of costs incurred over time, from the perspective of the payer, typically for a period of 1 year or more.

Costs can be attributed to specific sectors, such as costs for inpatient hospital care or costs paid to physicians for services covered under OHIP. Inpatient care and day surgery costs are computed using a top-down approach by multiplying the resource intensity weight of a stay (a measure of how much resources were used during the encounter) with cost per weighted case (which calculates the cost of a hypothetical, average Ontario patient each year; not the actual cost of a specific patient). As such, cost estimates of specific hospital encounters will be inaccurate (compared to cost estimates of all hospital encounters among the population). Additionally, this methodology means that costs associated with hospital stays cannot be partitioned into different components of the encounter (to isolate the costs of procedures of interest). Further, to ascertain costs for physicians for services billed under OHIP, we quantified the volume of services of urethral dilation, DVIU, and urethroplasty

procedures over the study period using select fee codes. Quantifying costs only for those fee codes would result in a partial cost estimate as other claims submitted during the encounter (outside of the codes used for study inclusion) are not enumerated.

Diagnostic codes for urethral stricture are not specific to site.

Codes Used for Cohort Creation		
Procedure	**Fee code**	**Description[a]**
Urethral dilation	Z612	Endoscopic urethral realignment for urethral trauma
	Z621	Urethra - Manipulation. Dilation of stricture. Local anaesthetic. Male.
	Z619	Urethra - Manipulation. Dilation of stricture. General anaesthetic. Male.
	Z615	Filiform and follower urethral dilation
DVIU	S532	Urethra - Incision. Urethrotomy. Transurethral (visual).
	S538	Urethra - Urethrotomy. Repeat procedure within 6 months by same surgeon.
	S531	Urethra - Incision. Urethrostomy.
Urethroplasty	S545	Urethra - Repair. Urethroplasty 1st. Stage. Posterior.
	S553	Urethra - Suture. Rupture. Posterior, late repair.
	S572	Male - Gen Sys. Hypospadias into glans using island flap pedicle (penoscrotal)
	S535	Urethra - Urethroplasty. 1st stage repair with/without skin graft.
	S558	Urethra - Urethroplasty. 2nd stage
	S550	Urethra - Repair. Urethroplasty. 1st stage-anterior.
	S552	Urethra - Suture. Posterior. Immediate repair.
	S578	Male - Gen Sys. Hypospadias with meatus to but not into glans.
	S571	Male - Gen Sys. Hypospadias with advancement of meatus into glans.
	S580	Male - Gen Sys. Hypospadias. Plastic reconstruction, urethra.
	Z604	Urethra - Incision. Meatotomy and plastic repair.
System	**Code**	**Description**
OHIP dxcode	598	Urethral stricture

[a]Source: https://www.ontario.ca/files/2025-03/moh-schedule-benefit-2025-03-19.pdf [accessed June 5, 2025].

Volume of Endoscopic Management (Usual Care) and Patient Characteristics Among Adult Men in Ontario – Fiscal Years 2022/23 and 2023/24		
	Patient with only 1 procedure (and no previous procedures in last 2 years)	**Patients with 1 or more procedures (or with previous procedures in last 2 years): the target population**
Endoscopic management volumes		
Patients with a urethral dilation and/or DVIU procedure	**N = 4,129**	**N = 1,503**
Characteristics of endoscopic management patients (at first record in observation period)		
Age – mean (SD)	67.61 (16.80)	69.66 (14.87)
Age – median (IQR)	71 (59-80)	73 (63-80)
OH region – Central – n	1,175 (28.5%)	410 (27.3%)
OH region – East – n	734 (17.8%)	275 (18.3%)
OH region – NE – n	187 (4.5%)	69 (4.6%)
OH region – NW – n	44 (1.1%)	16 (1.1%)
OH region – Toronto – n	936 (22.7%)	400 (26.6%)
OH region – West – n	1,053 (25.5%)	333 (22.2%)
Income quintile – missing – n	7 (0.2%)	1 (0.1%)
Income quintile – 1 (low income) – n	852 (20.6%)	338 (22.5%)
Income quintile – 2 – n	856 (20.7%)	339 (22.6%)
Income quintile – 3 – n	791 (19.2%)	295 (19.6%)
Income quintile – 4 – n	789 (19.1%)	262 (17.4%)
Income quintile – 5 (high income) – n	834 (20.2%)	268 (17.8%)
Material resources quintile – missing – n	32 (0.8%)	5 (0.3%)
Material resources quintile – 1 (low marginalization) – n	801 (19.4%)	282 (18.8%)
Material resources quintile – 2 – n	864 (20.9%)	275 (18.3%)
Material resources quintile – 3 – n	866 (21.0%)	327 (21.7%)
Material resources quintile – 4 – n	796 (19.3%)	296 (19.7%)
Material resources quintile – 5 (high marginalization) – n	770 (18.6%)	318 (21.2%)

Notes: Some values were suppressed due to re-identification risk. Proportions reflect column total.

Patient Volumes of Urethroplasty Among Adult Men in Ontario– by Fiscal Year	
FY	**N patients**
2015/16	168
2016/17	145
2017/18	184
2018/19	203
2019/20	212
2020/21	152
2021/22	171
2022/23	210
2023/24	210

Appendix 7: Estimation of the Population of Interest From Epidemiologic Data, Scenario

Table A14: Scenario From Epidemiologic Data – Uptake of Paclitaxel-Coated Balloon Dilation and Usual Care in Ontario: Adult Males With Recurrent Bulbar Urethral Strictures

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Current scenario						
Paclitaxel-coated balloon dilation[a]	–	–	–	–	–	–
Usual care	6,454	6,533	6,609	6,689	6,779	33,064
New scenario[b]						
Uptake rate for paclitaxel-coated balloon dilation	**20%**	**40%**	**60%**	**80%**	**100%**	**–**
Paclitaxel-coated balloon dilation	1,291	2,613	3,965	5,351	6,779	19,999
Usual care	5,163	3,920	2,644	1,338	-	13,065
Total	**6,454**	**6,533**	**6,609**	**6,689**	**6,779**	**33,064**

Note: Some numbers may appear inexact due to rounding.

[a]We assumed zero paclitaxel-coated balloon dilation procedures done in the current scenario and no expansion of patient population over time because of limited human health resources in urology.

[b]We calculated the volume of new interventions with paclitaxel-coated balloon dilation from the total number multiplied by the uptake rate of the intervention (starting from 20% in Year 1 and rising by 20% per year, achieving 100% in Year 5).

Appendix 8: Budget Impact Scenario Results: Population Estimated From Medical Services Data (OHIP Physician Claims)

Table A15A presents the overall budget impact of publicly funding paclitaxel-coated balloon dilation in the population of eligible adult men with recurrent bulbar urethral strictures (≤ 3 cm in length). The population was estimated by applying epidemiologic disease assumptions to the physician claims data (Table 29). The overall results are presented as Scenario 5 (S5), Table 33.

In the current scenario, using endoscopic management procedures for urethral dilation of recurrent bulbar urethral strictures, we estimated the total costs ranged from $3.15 million in year 1 to about $7.11 million in year 5, yielding a total 5-year cost of $26.83 million (treating about 3,911 adult men over 5 years).

Assuming a rapid uptake of paclitaxel-coated balloon dilation in the new scenario, starting from 50% in year 1 and increasing to 100% by year 5, the estimated total costs ranged from $3.53 million to $6.31 million per year over the next 5 years, with a total 5-year cost of $25.84 million (treating about 3,080 adult men with the paclitaxel-coated balloon catheter over 5 years).

The 5-year net budget impact of publicly funding the paclitaxel-coated balloon dilation procedure was cost saving (−$0.99 million), with additional costs of $0.38 million shown for year 1 and annual savings for the remaining years ranging from $0.02 million to $0.80 million.

Table A15A: Budget Impact Scenario Results (Estimation of Population Based on Physician Claims Data)

	Annual and total costs and budget impact, $ million[a]					
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total[b,c]**
Current scenario, overall	**3.15**	**4.75**	**5.51**	**6.30**	**7.11**	**26.83**
Usual care	3.15	4.75	5.51	6.30	7.11	26.83
Paclitaxel-coated balloon dilation	–	–	–	–	–	–
New scenario, overall	**3.53**	**4.73**	**5.35**	**5.90**	**6.31**	**25.84**
Usual care	1.58	1.89	1.52	1.03	0.75	6.77
Paclitaxel-coated balloon dilation	1.96	2.85	3.83	4.87	5.56	19.06
Budget impact[b,c]	**0.38**	**−0.02**	**−0.16**	**−0.40**	**−0.80**	**−0.99**

[a]All costs in 2025 CAD.

[b]Negative costs indicate savings.

[c]Results may appear inexact due to rounding. Budget impact calculated as the difference between the total costs in the new and current scenarios.

Table A15B presents reference case budget impact over the next 5 years by the cost component. The highest cost component, also associated with additional costs of about $9.97 million over 5 years was the cost of the paclitaxel-coated balloon dilation procedure including the cost of the device. As mentioned above, the estimated cost savings with the new scenario of about $0.99 million over the next 5 years resulted from the reductions in downstream treatment costs, for example:

- reductions in the costs of follow-up care with urethral dilation in people who were not successfully treated with endoscopic management with 5-year cost savings of about $1.72 million, or
- reductions in the imminent need of urethroplasty, yielding the cost savings of about $7.20 million over the next 5 years

Table A15B: Budget Impact Scenario Results by Cost Component (Estimation of Population Based on Physician Claims Data)

Scenario	Annual and total costs and budget impact, $ million[a]					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total[b,c]
Current scenario	**3.15**	**4.75**	**5.51**	**6.30**	**7.11**	**26.83**
Endoscopic management: overall procedure cost	0.96	0.99	1.02	1.05	1.08	5.11
Device cost: Optilume	0.00	0.00	0.00	0.00	0.00	0.00
Recurrence: Costs of FU care with urethral dilation	0.08	0.36	0.66	0.97	1.28	3.36
Recurrence: Costs of FU care with ISD or indwelling catheter	0.01	0.03	0.06	0.08	0.11	0.28
Urethroplasty	1.70	2.60	2.68	2.75	2.83	12.57
Other health care costs	0.39	0.76	1.10	1.44	1.81	5.50
New scenario: Overall	**3.53**	**4.73**	**5.35**	**5.90**	**6.31**	**25.84**
Endoscopic management: overall paclitaxel-coated balloon dilation procedure cost	2.16	2.59	3.05	3.52	3.76	15.09
Device cost: Optilume[d]	1.03	1.38	1.75	2.14	2.32	8.62
Recurrence: Costs of FU care with urethral dilation	0.05	0.21	0.35	0.47	0.56	1.64
Recurrence: Costs of FU care with ISD or indwelling catheter	0.00	0.02	0.03	0.04	0.05	0.14
Urethroplasty	1.02	1.38	1.19	0.95	0.83	5.37
Other health care costs	0.30	0.54	0.74	0.92	1.11	3.61
Overall budget impact[b,c,d]	**0.38**	**-0.02**	**-0.16**	**-0.40**	**-0.80**	**-0.99**
Budget impact: overall procedure cost	1.19	1.60	2.03	2.47	2.68	9.97
Budget impact: device cost [d]	1.03	1.38	1.75	2.14	2.32	8.62
Budget impact: Costs of FU care with urethral dilation	−0.03	−0.16	−0.31	−0.50	−0.72	−1.72
Budget impact: Costs of FU care with ISD or indwelling catheter	0.00	−0.01	−0.03	−0.04	−0.06	−0.15
Budget impact: Urethroplasty	−0.68	−1.22	−1.49	−1.81	−2.00	−7.20
Budget impact: Other healthcare costs	−0.10	−0.22	−0.36	−0.52	−0.70	−1.90

Abbreviations: FU, follow up; ISD, intermittent self-dilatation (self-catheterization).

[a]All costs in 2025 CAD.

[b]Negative costs indicate savings.

[c]Results may appear inexact due to rounding.

[d]Device costs included in the overall paclitaxel-coated balloon dilation procedure cost.

Appendix 9: Letter of Information

LETTER OF INFORMATION

Ontario Health

Ontario Health is conducting a review of **Optilume.** The purpose is to better understand whether this intervention should be publicly funded in Ontario.

An important part of this review involves gathering perspectives of patients and caregivers of those who have been diagnosed with urethral strictures who may or may not have experience with paclitaxel-coated balloon catheter (Optilume).

WHAT DO YOU NEED FROM ME

- ✓ Willingness to share your story
- ✓ 30-40 minutes of your time for a phone interview
- ✓ Permission to audio- (not video-) record the interview

WHAT YOUR PARTICIPATION IN VOLVES

If you agree to share your experiences, you will be asked to have an interview with Ontario Health (OH) staff. OH staff will contact interested participants by collecting contact information (i.e., email address and/or phone number) to set up an interview. The interview will last about 30-40 minutes. It will be held over the telephone. With your permission, the interview will be audio-taped. The interviewer will ask you questions about you or your loved one's condition and your perspectives about your diagnosis and treatment options in Ontario. Participation is voluntary. You may refuse to participate, refuse to answer any questions or withdraw before or at any point during your interview. Withdrawal will in no way affect the care you receive.

CONFIDENTIALITY

All information you share will be kept confidential and your privacy will be protected except as required by law. The results of this review will be published, however no identifying information will be released or published. Any records containing information from your interview will be stored securely until a year after the project completion. After a year post completion, the records will be destroyed. If you are sending us personal information by email, please be aware that electronic communication is not always secure and can be vulnerable to interception.

Ontario Health is designated an "institution" by the *Freedom of Information and Protection of Privacy Act* (FIPPA) and is collecting your personal information pursuant to FIPPA and the *Connecting Care Act, 2019* to support the Health Technology Assessment Program. If you have any questions regarding Ontario Health's collection and use of personal information for the purposes of this program, please contact Team Lead, Jigna Mistry noted below.

RISKS TO PARTICIPATION

There are no known physical risks to participating. Some participants may experience discomfort or anxiety after speaking about their experience.

IF YOU ARE INTERESTED, PLEASE CONTACT US:

DOCUMENTATION OF INFORMED CONSENT

We will give you a copy of this informed consent form after you and the OH staff have signed and dated it.

By signing this form, you confirm that:

- You agree to participate in this interview.
- You understand that your participation is voluntary.
- You understand the purpose, activities, risks and benefits of participating in this interview.
- You authorize the OH staff to use your data as explained in this form.
- OH staff have answered your questions to your satisfaction.

Please check the appropriate boxes:

- You give permission to the OH staff to audio record your interview: YES ☐ NO ☐

Name of Participant (please print):

_____

Signature of Participant (please sign):

_____

Name of OH Staff:

_____

Signature of OH Staff:

_____

Place: _____

Date: _____

Note: For participants who are unable to electronically sign the consent form with their permission to participate in this interview, OH staff will audio-record participants' consent prior to their interview and retain a record of participants' verbal consent through OH's dedicated secure network drive.

Appendix 10: Interview Guide

Paclitaxel-Coated Balloon Dilation Interview Guide

Diagnosis and Burden of Disease

1. What symptoms have you experienced related to urethral strictures, and how long ago were you diagnosed?
2. How have urethral strictures affected your daily life, work, relationships, mental health, and overall quality of life?
3. What treatments have you tried, and what was your experience with them (e.g. effectiveness, side effects, pain)?

Experience with Optilume (Paclitaxel-Coated Balloon Dilation)

1. Were you aware of Optilume before considering it?
2. What factors influenced your decision to undergo Optilume (e.g. physician advice, comparing alternative treatment options etc.)?
3. What was your experience before, during, and after the procedure, including follow-up care?
4. Did you face any barriers accessing Optilume (e.g. cost, location, wait times)?
5. What impact did Optilume have on your symptoms or recurrence of strictures?

No Experience with Optilume (Paclitaxel-Coated Balloon Dilation)

1. Are you aware of Optilume? If yes, how did you hear about it?
2. What factors would you consider if deciding whether to undergo Optilume (e.g. physician advice, comparing alternative treatment options etc.)?

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About Us

We are an agency created by the Government of Ontario to connect, coordinate, and modernize our province's health care system. We work with partners, providers, and patients to make the health system more efficient so everyone in Ontario has an opportunity for better health and well-being.

Equity, Inclusion, Diversity and Anti-Racism

Ontario Health is committed to advancing equity, inclusion and diversity and addressing racism in the health care system. As part of this work, Ontario Health has developed an Equity, Inclusion, Diversity and Anti-Racism Framework, which builds on existing legislated commitments and relationships and recognizes the need for an intersectional approach.

Unlike the notion of equality, equity is not about sameness of treatment. It denotes fairness and justice in process and in results. Equitable outcomes often require differential treatment and resource redistribution to achieve a level playing field among all individuals and communities. This requires recognizing and addressing barriers to opportunities for all to thrive in our society.

For more information about Ontario Health, visit OntarioHealth.ca.

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