ORIGINAL RESEARCH

# The sublingual vaccine MV140 is dominant over prophylactic antibiotics for the prevention of recurrent, uncomplicated urinary tract infections in adult women

## A cost-utility analysis

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## ABSTRACT

**INTRODUCTION:** Recurrent, uncomplicated urinary tract infections (rUTIs) in women are associated with burdensome symptoms, high antibiotic use, and significant costs. The sublingual vaccine MV140 has demonstrated significant reduction in rUTI rates in Canada and Europe. This analysis examined the cost-effectiveness of MV140 as an alternative to prophylactic antibiotics (pAbs) for rUTI prevention in adult women in the Canadian healthcare setting.

**METHODS:** A cost-utility model was developed to follow rUTI patients over 1.25 years through four health states: UTI-free survival, acute UTI, pyelonephritis, and death. A decision tree was used to model the acute UTI state, accounting for Ab resistance and choice of first-line Ab treatment, while Markov model transition probabilities were derived from a published direct comparison. Cost inputs included drug acquisition/administration, healthcare resource use, adverse events, and lost productivity, and were based on Canadian governmental resources. Utilities were derived from published literature. The base case was probabilistic (n=5000); multiple one-way sensitivity analyses were performed to assess model uncertainty.

**RESULTS:** MV140 was associated with cost-savings (-$1442) and increased quality of life years (0.01) compared to pAbs, with an incremental cost-effectiveness ratio of -$229 088 in the base case (societal perspective). MV140 remained dominant over pAbs in most scenario analyses, with incremental costs ranging from -$256 207 to $875.

**CONCLUSIONS:** MV140 represents a consistently cost-effective alternative to pAbs in the Canadian healthcare system. When societal costs are considered, MV140 is consistently dominant over pAbs irrespective of variation in scenario inputs, demonstrating the considerable economic value of MV140 in this disease setting.

## INTRODUCTION

Urinary tract infections (UTIs) are the most common bacterial infections worldwide, with over half of all women reporting at least one UTI in their lifetime.[1] The majority of UTIs are uncomplicated (uUTIs), occurring in otherwise healthy, non-pregnant women with no urinary system abnormalities; however, despite the low mortality risk of uUTIs, these infections are still associated with significant disease burden. Persistent uUTIs can progress to pyelonephritis, although rarely, which is associated with additional symptoms, including fever and vomiting; if left untreated, serious complications (including sepsis and renal failure) may ensue.[2]

The landscape of UTIs is further complicated by the occurrence of recurrent UTIs (rUTIs), commonly defined as three or more culture-documented infections within a 12-month period.[1] Increased healthcare resource utilization due to rUTI can lead to significant healthcare system burden due to the high prevalence of this condition, while symptom recurrence can be a key source of discomfort and stress for patients.[3,4]

Although current antibiotic treatment strategies are generally effective at resolving acute cases of UTI, patients with rUTI commonly experience significant negative impacts on their quality of life, including depression, inability to engage in sexual activity, and loss of work productivity.[5-9] Furthermore, the possibility of

## KEY MESSAGES

- A cost-utility analysis comparing the sublingual vaccine MV140 to prophylactic antibiotics in rUTIs from a Canadian societal perspective was conducted.
- Key cost categories evaluated include medication costs, tests and medical visits, adverse events, and lost productivity.
- MV140 is dominant over prophylactic antibiotics for the prevention of recurrent, uncomplicated UTI in adult women, demonstrating economic value in rUTI.
- MV140 presents consistent cost-effectiveness at a willingness-to-pay threshold of $50 000/quality of life year as compared to prophylactic antibiotics in all scenario analyses.

resistance to available treatments is a substantial source of patient anxiety, as well as a growing public health concern.[5,7]

Prophylactic antibiotic (pAbs) are the mainstay of preventative treatment for rUTI; however, pAbs pose multiple safety concerns in the form of high adverse event incidence and the development of multi-antibiotic resistance.[10,11] Women with rUTIs express concerns regarding adverse events, other infections, and loss of efficacy for pAbs in the long term, leading to usage of alternative treatments with unproven efficacy.[12] Patients must also remain on pAbs in the long term to ensure that infections do not return, with multiple studies and patient-provided perspectives reporting loss of efficacy as soon as pAb treatment courses cease.[7,9] The negative effects of antibiotic prophylaxis are further elevated in older adults with rUTIs, who experience increased risks of hospital visits, diarrhea, side effects, and antibiotic resistance as compared to patients who did not receive pAbs.[13]

The sublingual vaccine MV140 represents a novel, non-antibiotic, prophylactic treatment option for rUTI patients. In a recent study by Lorenzo-Gomez et al, patients on MV140 were four times less likely to develop a UTI than those on pAb treatment, with significant reductions in the mean number of UTIs throughout the study period (1.35, 95% confidence interval [CI] 1.15–1.54] vs. 5.75, 95% CI: 5.37-6.13) for MV140 patients (n=159) as compared to pAb patients (n=160).[14]

Similarly, another recent study by Lorenzo-Gomez et al indicated an absolute risk reduction of 90% for MV140 patients (n=360) as compared to pAb patients (n=339) for UTI development. The majority of MV140 patients remained UTI-free over the 12-month period following cessation of treatment, while all pAb patients experienced a UTI within 12 months after prophylactic treatment ceased.[15]

In the Canadian setting, a recent prospective case study of 64 adult women with rUTI demonstrated a 75.9% reduction in monthly UTI rates per subject in the nine-month efficacy period following MV140 vaccination, with a 40.6% UTI-free rate.[16] The pivotal randomized placebo controlled trial (NCT02543827) confirmed the value of MV140 in lowering UTI episodes and prolonging UTI-free time, with significant improvements in quality of life (compared to placebo) and no serious adverse events related to study drug.[1]

Given the increasing prevalence of UTI across the globe, it is crucial to ensure that patients have access to safe and effective non-antibiotic methods of prophylaxis to prevent further increases in antibiotic resistance and associated morbidity, mortality, and healthcare system burden. The objective of this cost-utility analysis was to determine the cost-effectiveness of MV140 relative to pAbs as a prophylactic treatment for the prevention of rUTIs from a Canadian societal perspective.

## METHODS

### Model structure

A half-cycle corrected Markov model was developed to assess the cost-effectiveness of MV140 as compared to pAbs, with an embedded underlying decision tree to model outcomes associated with persistent infections. The time horizon of the model is 1.25 years, reflecting the duration of the published direct comparison study,[14] and the cycle length is 14 days. Costs and outcomes are discounted at a rate of 1.5% per annum. The Markov model follows patients through four health states: UTI-free survival (UFS), acute UTI, pyelonephritis, and death (Figure 1).

To account for the effects of antibiotic resistance and second-line antibiotic treatment in acute UTI, a decision tree is used to inform costs and outcomes associated with the acute UTI health state (Figure 2).

### Patient population

All patients entering the model are adult female rUTI patients and are assumed to receive a full course of prophylactic treatment to prevent further infections;

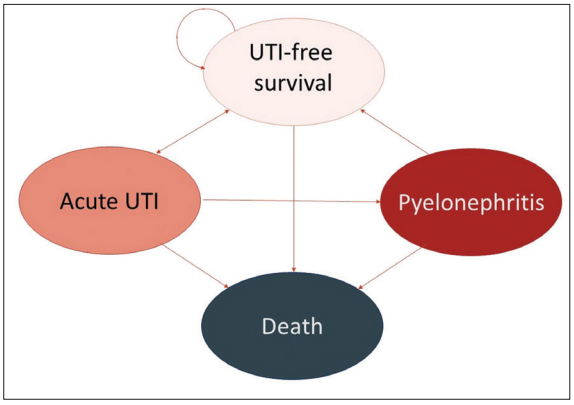


**Figure 1.** Markov model diagram. Patients enter the model in the urinary tract infection (UTI)-free survival (UFS) health state and can freely transition to acute UTI. Acute UTI patients may either resolve their infection within one model cycle or develop pyelonephritis; pyelonephritis patients will resolve within one model cycle. Death, the absorption health state, occurs at the natural mortality rate.

as such, all patients are assumed to begin in the UFS health state and are commencing treatment in either prophylactic arm (MV140 or pAbs). Patients enter the model at a starting age of 47.9 years, in alignment with the mean age of patients in the published direct comparison used to inform Markov transition probabilities in this analysis.[14]

## Comparators

The selection of pAbs used in the model is informed both by Canadian clinical experience and the published American Urological Association/Canadian Urological Association (AUA/CUA) guidelines.[17] Each pAb (cephalexin, fosfomycin, nitrofurantoin, trimethoprim [TMP], or TMP/sulfamethoxazole [SMX]) has an equal chance of being used for preventative treatment.

Adjunct therapies, including vaginal estrogens for postmenopausal women and lifestyle changes, are assumed to be used at equal frequencies in both treatment arms, and are not factored into the economic model.

For cost calculation purposes, it is assumed that all patients on pAbs receive continuous prophylaxis for the entire six-month duration of prophylactic treatment, and are compliant with their treatment regimen; similarly, it is assumed that all patients on MV140 are compliant with treatment for the three-month treatment period.

## Transition probabilities

Markov transition probabilities informing health occupancy in each state are derived from published literature and are summarized in Table 1. Whether through resolution and return to the UFS health state, or through transition to the pyelonephritis health state, acute UTI is assumed to resolve within one model cycle. Similarly, the

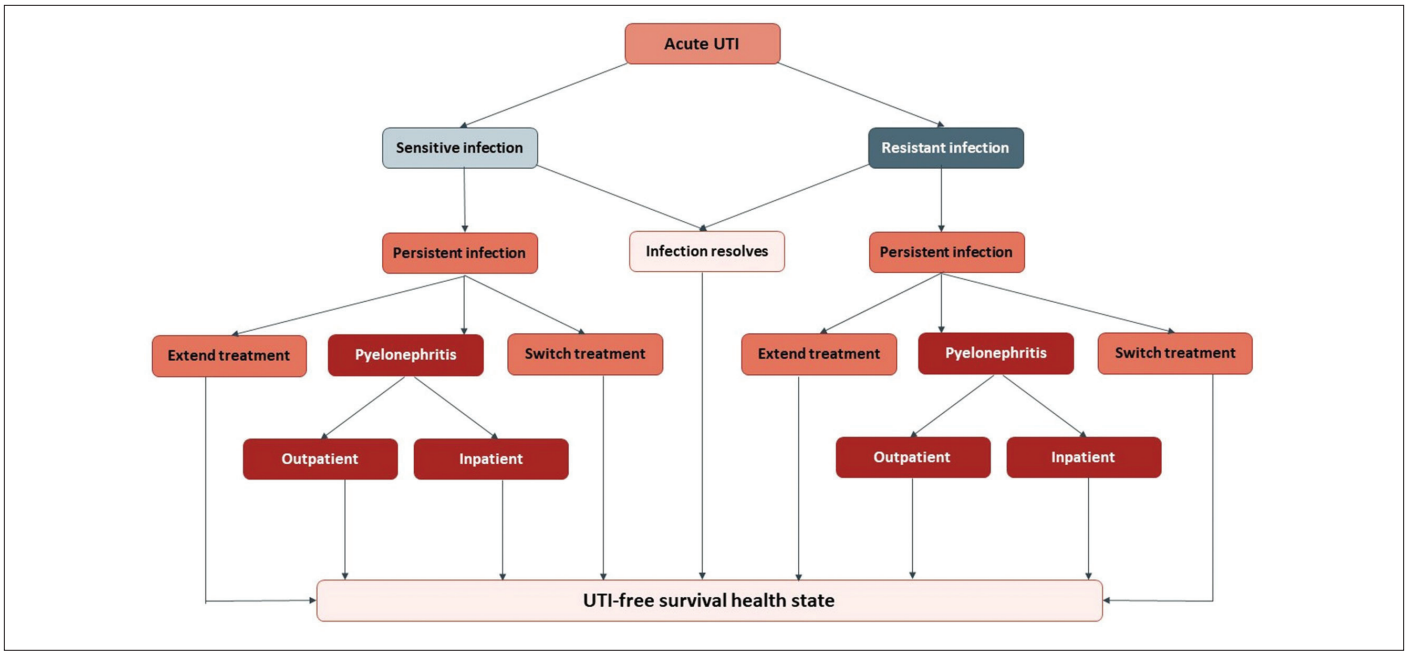


**Figure 2.** Decision tree used to calculate costs and outcomes in the acute urinary tract infection (UTI) health state. Patients developing acute UTI may have their infection resolve after treatment with a first-line antibiotic (depending on whether the infection is resistant or sensitive to the first-line antibiotic used to treat) or persist. Persistent patients have a small chance of developing pyelonephritis; those who do not will move on to a second-line antibiotic, which may either be an extension of first-line treatment, or a switch to an alternate antibiotic. All acute UTI patients resolve their infection within one model cycle. Acute UTI-associated costs and outcomes are calculated only for non-pyelonephritis patients.

**Table 1. Health state transition probabilities for patients on MV140 or prophylactic antibiotics**

| | Ending health state | | |
|---|---|---|---|
| Starting health state | UFS | Acute UTI | Pyelonephritis |
| MV140 | | | |
| UFS (0–3 months)[14] | 94.6% | 5.4% | 0.0% |
| UFS (3–6 months)[14] | 97.3% | 2.7% | 0.0% |
| UFS (6–9 months)[14] | 97.3% | 2.7% | 0.0% |
| UFS (9+ months)[14] | 95.4% | 4.6% | 0.0% |
| Acute UTI[19-22] | 99.4% | 0.0% | 0.6% |
| Pyelonephritis | 100.0% | 0.0% | 0.0% |
| Prophylactic antibiotics | | | |
| UFS (0–3 months)[14] | 78.2% | 21.8% | 0.0% |
| UFS (0–3 months)[14] | 85.1% | 14.9% | 0.0% |
| UFS (0–3 months)[14] | 85.1% | 14.9% | 0.0% |
| UFS (0–3 months)[14] | 85.5% | 14.5% | 0.0% |
| Acute UTI (on treatment)[19-23] | 99.3% | 0.0% | 0.7% |
| Acute UTI (off treatment)[19-23] | 99.4% | 0.0% | 0.6% |
| Pyelonephritis | 100.0% | 0.0% | 0.0% |

Death, the absorption health state, is unrelated to uncomplicated UTI, and occurs at the natural mortality rate. UFS: UTI-free survival; UTI: urinary tract infection.

pyelonephritis health state is assumed to resolve within one model cycle through return to the UFS health state. Death, the absorption health state, is unrelated to uUTI and is assumed to occur at the natural mortality rate, as informed by Canadian life tables from Statistics Canada.[18]

The probability of developing an acute UTI from the UFS health state is derived from a published direct comparison.[14] Probabilities of developing pyelonephritis from this health state are calculated from the decision tree;[19-22] however, patients on pAbs exhibit a higher chance of pyelonephritis development due to Ab resistance arising from long-term Ab exposure. Therefore, odds ratios from published literature of 2.48 for pAb patients on prophylactic treatment and 1.33 for pAb patients off prophylactic treatment were applied.[23]

Decision tree probabilities are independent of the type of prophylactic treatment received. Patients with acute UTI receive first-line Ab treatment, whose efficacy is determined by bacterial pathogen distribution, first-line Ab usage frequencies, and Ab resistance rates; should the infection persist, patients may either extend their first-line therapy or switch to a second-line Ab. Probabilities informing the decision tree are summarized in Table 2. Costs and outcomes associated with the acute UTI health state are calculated based on the 99.43% of patients who will resolve their infections within one model cycle (i.e., those who do not develop pyelonephritis).[19-22]

## Utilities

Health state utilities used in this analysis are derived from published cost-effectiveness analyses for UTI, and are based on the Quality of Well-Being Scale.[3,24] UFS utilities are based on an average of reported utilities for resolved UTI post-first-line or second-line treatment, while acute UTI utilities are calculated based on progression through the decision tree.

Disutility values are derived from cost-utility publications in the diabetes or uterine fibroid disease settings.

Utility and disutility values are summarized in Table 3.

## Costs

Where applicable, all costs are inflated to 2022 values using the Canadian Consumer Price Index.[25]

Unit costs for all antibiotics are sourced from the Ontario Drug Benefit (ODB) e-formulary and the British Columbia (BC) PharmaCare Formulary, as a proxy for the rest of Canada.[26,27] The administration costs associated with intravenous antibiotics are sourced from the Ontario Schedule of Benefits (OSB) as a proxy for the rest of Canada.[28] The vial price of MV140 has been estimated based on input from the manufacturer. Wastage is factored into all drug price calculations.

Test and medical visit costs included in the model are health-state specific, and factor in the proportion of pyelonephritis patients expected to be treated in the inpatient setting. All patients with acute UTI receive urinalysis and a urine culture, while approximately half of patients require imaging (in the form of a pelvic ultrasound) or cystoscopy. Patients with pyelonephritis will receive urinalysis and a urine culture, with the majority also performing a blood culture, a complete blood count, and a creatinine test, and approximately half receiving imaging (either by pelvic or renal ultrasound). Unit costs for all tests are derived from the OSB or the Ontario Schedule of Benefits for Laboratory Services as a proxy for the rest of Canada.[28,29]

Patients in the UFS health state do not require disease-specific medical visits, while acute UTI patients are assumed to visit a urologist at the beginning of their infection, with some patients having a followup visit with either their general practitioner (GP) or urologist. Pyelonephritis inpatients require hospitalization, with a

**Table 2. Decision tree probabilities informing costs and outcomes in the acute UTI health state**

| Parameter | Probability |
|---|---|
| Distribution of causative bacteria for acute UTIs | |
| *E.coli* | 84.1%[21] |
| *K. pneumoniae* | 3.8%[21] |
| *P. vulgaris* | 2.6%[21] |
| *E. faecalis* | 2.8%[21] |
| Other | 6.7%[21] |
| Probability of acute UTI resolving when treated with a 1st-line antibiotic | |
| Ciprofloxacin (Ab-sensitive infection, scenario) | 94.0%[44-46] |
| Ciprofloxacin (Ab-resistant infection, scenario) | 78.0%[44-46] |
| Fosfomycin (Ab-sensitive infection) | 94.0%[44-46] |
| Fosfomycin (Ab-resistant infection) | 54.0%[44-46] |
| Nitrofurantoin (Ab-sensitive infection) | 85.0%[44-46] |
| Nitrofurantoin (Ab-resistant infection) | 53.6%[44-46] |
| TMP/SMX (Ab-sensitive infection) | 91.0%[44-46] |
| TMP/SMX (Ab-resistant infection) | 55.0%[44-46] |
| Overall resistance rate for 1st-line Abs | |
| Ciprofloxacin (scenario) | 19.5%[20] |
| Fosfomycin | 0.6%[21] |
| Nitrofurantoin | 13.1%[22] |
| TMP/SMX | 24.0%[20] |
| Resistant acute UTIs after 1st-line antibiotics | |
| Chance of extending 1st-line Ab | 24.0%[19-22] |
| Chance of switching to a different 2nd-line Ab | 72.0%1[9-22] |
| Chance of developing pyelonephritis | 4.0%[19-22] |

Ab: antibiotic; TMP/SMX: trimethoprim/sulfamethoxazole; UTI: urinary tract infection.

small percentage needing abscess surgery; outpatients are managed through emergency room (ER) visits and may require more than one visit for management. Unit costs for medical visits are derived from the OSB, the Canadian Institute for Health Information (CIHI) Patient Cost Estimator (PCE), the Government of Canada Job Bank, the CIHI Comprehensive Ambulatory Classification System (CACS), and the Ontario Case Costing Initiative (OCCI).[28,30-34]

Adverse event (AE) cost calculations assume that all patients experiencing AEs are treated in an outpatient setting, as all reported AEs are mild, and thus are not deemed severe enough to require inpatient care. Costs per episode are therefore derived from the cost of one GP visit as per the OSB,[28] with additional cost for AE-associated medications if specific treatment is typically provided. These are applied as a one-time cost in the first model cycle.

Lost time costs in the economic model are attributable to three primary categories: tests and medical visits, AEs, and additional sick leave days for recovery from illness. Each medical visit is assumed to require four hours of time, including transportation to and from the hospital and waiting time; medical tests are assumed to have shorter time requirements, and require two hours of time. Each AE is associated with four hours of lost time, or the length of time associated with one medical visit; AE costs are applied as one-time costs in the first model cycle.

Lost time due to recovery is based on a European study, which found that female rUTI patients required an additional 3.09 days of sick leave per year due to their UTIs; based on a patient population with five UTIs per year and an eight-hour working day, it was calculated that 4.94 hours of recovery time are associated with each acute UTI or outpatient pyelonephritis event. Pyelonephritis patients who require inpatient treatment will also lose time corresponding

**Table 3. Utility and disutility values**

| Parameter | (Dis)utility |
|---|---|
| Utility values | |
| UTI-free survival | 0.825[3] |
| Acute UTI | 0.775[3] |
| Pyelonephritis | 0.590[24] |
| Adverse event disutility values | |
| Abdominal pain/dyspepsia | -0.034[47] |
| Diarrhea | -0.034[47] |
| GI symptoms (nausea) | -0.034[47] |
| Lower respiratory tract infection | -0.010[48] |
| Pain | -0.060[48] |
| Pruritus | -0.014[48] |
| Skin rash | 0.000[48] |
| Vaginal/oral candidiasis | -0.038[47] |

Utility values for the acute UTI health state are derived from weighted half-cycle utility values calculated in the decision tree. GI: gastrointestinal; UTI: urinary tract infection.

**Table 4. Results of the base case probabilistic analysis**

| Parameter | MV140 | pAbs | Incremental |
|---|---|---|---|
| Costs | | | |
| Drug acquisition | $1145.73 | $225.15 | $920.58 |
| Tests & medical visits | $337.34 | $1233.43 | -$896.09 |
| Adverse events | $3.32 | $31.61 | -$28.29 |
| Lost productivity | $539.30 | $1977.93 | -$1438.63 |
| Total | $2025.69 | $3468.12 | -$1422.43 |
| Benefits | | | |
| LYs in UFS | 1.18 | 1.05 | 0.12 |
| LYs in acute UTI | 0.05 | 0.17 | -0.12 |
| LYs in pyelonephritis | 0.00 | 0.00 | 0.00 |
| Total LYs | 1.22 | 1.22 | 0.00 |
| QALYs in UFS | 0.97 | 0.87 | 0.10 |
| QALYs in acute UTI | 0.04 | 0.13 | -0.09 |
| QALYs in pyelonephritis | 0.00 | 0.00 | 0.00 |
| Disutility | 0.00 | -0.01 | 0.01 |
| Total QALYs | 1.01 | 1.00 | 0.01 |

Numbers may appear off due to rounding. LYs: life years; pAbs: prophylactic antibiotics; QALYs: quality of life years; UFS: UTI-free survival; UTI: urinary tract infection.

to the average length of their hospital stay; as per the OCCI, pyelonephritis-associated hospitalization has a duration of five days, where each day encompasses eight hours of lost time.

All unit costs used in this model are summarized in Supplementary Table 1 (available at *cuaj.ca*).

## Sensitivity analyses

Probabilistic and deterministic scenario analyses have been conducted to determine the robustness of the model to parameter variation. The base case of the model has been run probabilistically at 5000 iterations to assess the effect of model parameter uncertainty, and one-way deterministic sensitivity analyses have been conducted to identify the parameters that influence the cost-utility ratio to the greatest degree.

Additional probabilistic scenario analyses at 1000 iterations have been carried out to reflect key clinical scenarios that may be observed in treatment practice. These include: a truncated time horizon, the public health system perspective, a 'community setting' in which ciprofloxacin is used as a first-line antibiotic and in which community pharmacists may prescribe acute UTI medication, a scenario in which nitrofurantoin use is favored (50% usage) due to its lower risk of side effects

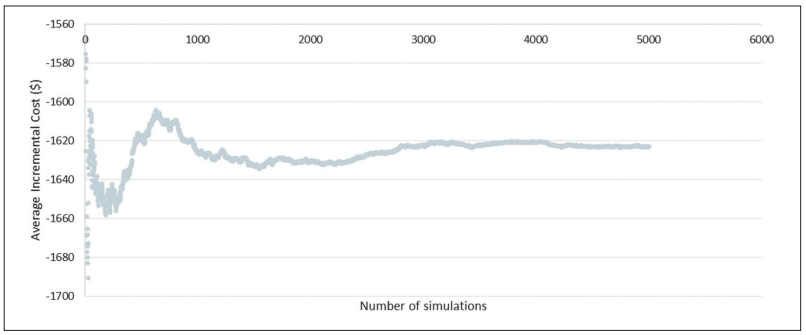


**Figure 3.** Cost convergence plot for probabilistic analysis (n=5000). The average incremental cost is consistent across probabilistic simulations and stabilizes fully at fewer than 1000 iterations.

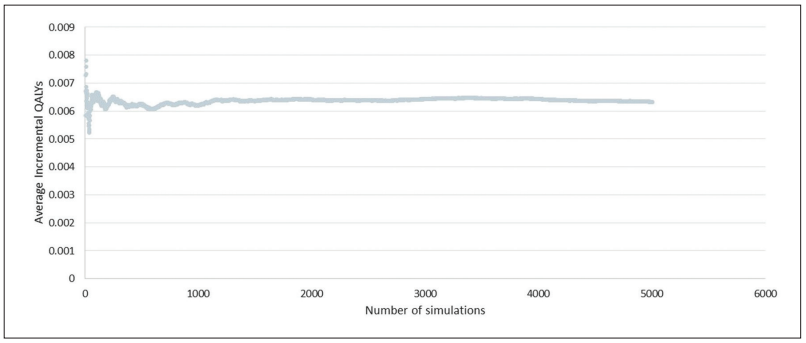


**Figure 4.** Benefit convergence plot for probabilistic analysis (n=5000). The average incremental benefit, depicted in quality of life years (QALYs), is fairly consistent across probabilistic simulations and stabilizes fully at fewer than 1000 iterations.

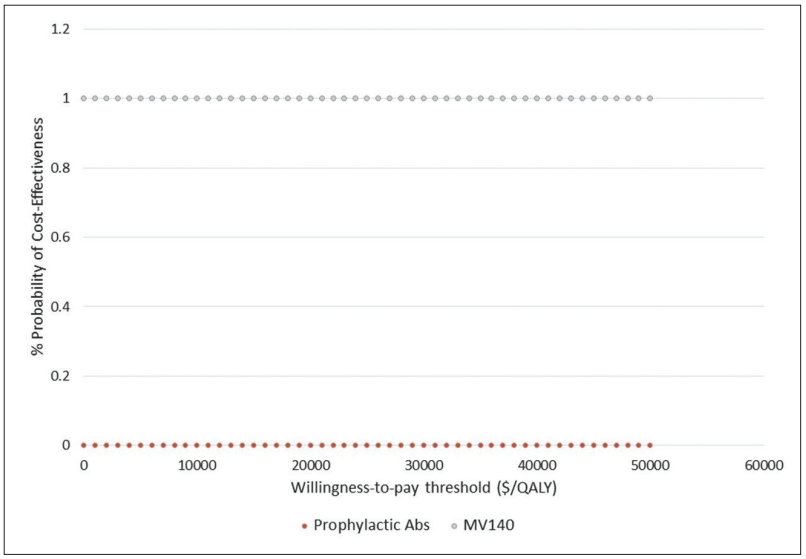


**Figure 5.** Cost-effectiveness acceptability curve for MV140 vs. prophylactic antibiotics (pAbs). The probability of cost-effectiveness, based on net monetary benefit, is displayed across willingness-to-pay thresholds ranging from $0/QALY to $50 000/QALY. QALY: quality of life years.

as per real-world prescribing patterns,[4] an exploration of alternate transition probabilities,[1,35] and a scenario in which pAbs lose efficacy post-treatment.

## RESULTS

In the base case, treating patients with MV140 would result in total discounted costs of $2025.69, as compared to $3468.12 for pAbs. Over a 1.25-year time horizon, treatment with MV140 would result in 1.22 discounted life years (LYs) and in 1.01 discounted quality of life years (QALYs), while pAbs produce discounted LYs of 1.22 and discounted QALYs of 1.00 (Table 4). The incremental cost-utility ratio was -$229 087.60/QALY, with MV140 exhibiting dominance over pAbs.

In general, the model exhibits convergence at fewer than 1000 iterations for both incremental costs and incremental benefits (Figures 3, 4). MV140 is dominant over pAbs and is considered the more cost-effective treatment at a willingness-to-pay threshold of $50 000/QALY in approximately 100% of iterations (Figure 5). A scatterplot depicting incremental costs and QALYs across all base case iterations is provided in Figure 6.

MV140 remains dominant over pAbs in all one-way sensitivity analyses conducted. Based on the results of this analysis, the model is most sensitive to changes in utility values, starting age, and time horizon (Figure 7).

In all probabilistic scenarios, the model results are consistent, with MV140 exhibiting cost-effectiveness as compared to pAbs regardless of variation in scenario inputs. Overall, QALYs are most sensitive to changes in transition probabilities, while costs are most sensitive to changes in time horizon, perspective, and transition probabilities; in scenario analyses where these inputs are not varied, changes in costs and QALYs are within 25% of the base case probabilistic result (Table 5).

**Table 5. Results of probabilistic scenario analyses**

| Scenario | Incremental costs ($) | Incremental QALYs | ICUR ($/QALY) |
|---|---|---|---|
| 1-year time horizon | -$1066.73 | 0.005 | -$196 556.54 |
| Public payer perspective | $5.79 | 0.007 | $874.69 |
| Community health setting | -$1400.84 | 0.006 | -$232 551.39 |
| pAbs lose all efficacy after treatment ends | -$2102.02 | 0.008 | -$256 207.18 |
| Nitrofurantoin use is favored | -$1423.02 | 0.006 | -$229 854.79 |
| Alternate transition probabilities* | -$576.98 | 0.004 | -$141 404.60 |

Numbers may appear off due to rounding. *Alternate transition probabilities referred to are: 0% and 8% in months 0–6 and 6–15, and 1.6% and 20.81% in months 0–6 and 6–15 for MV140 and pAbs, respectively. ICUR: incremental cost-utility ratio; pAbs: prophylactic antibiotics; QALYs: quality of life years.

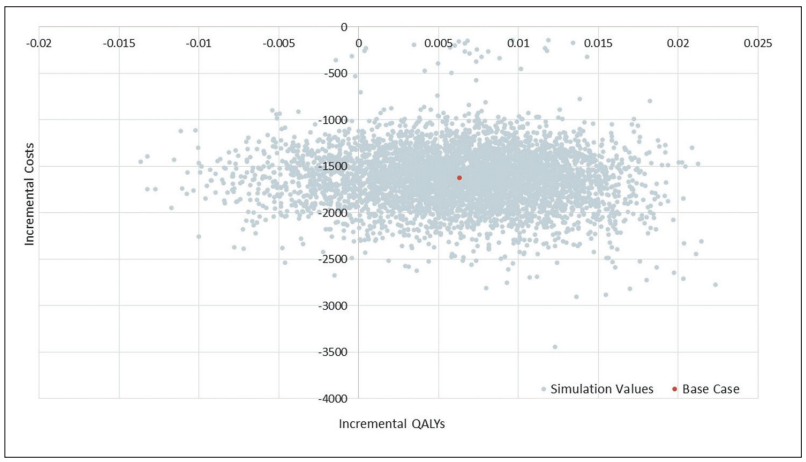


**Figure 6.** Cost-effectiveness plane for MV140 vs. prophylactic antibiotics (pAbs). Incremental costs and quality of life years (QALYs) for MVV140 vs. pAbs are depicted for each probabilistic simulation (n=5000) in blue dots. The base case is represented by a red dot.

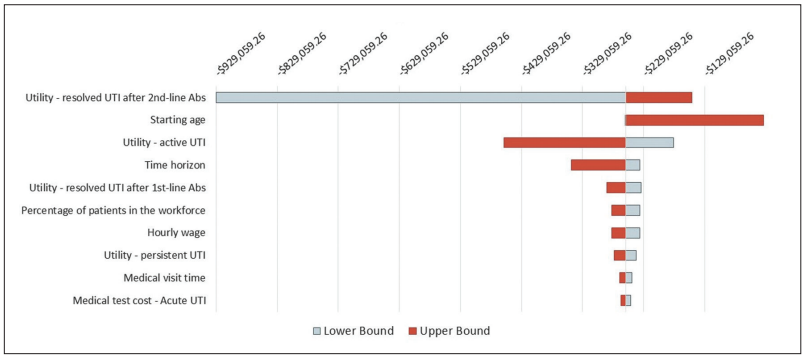


**Figure 7 .** One-way deterministic sensitivity analyses (DSA) for MV140 vs. prophylactic antibiotics (pAbs). The tornado plot depicts the deterministic incremental cost utility ratio (ICUR) resulting from ±10% variation in the specified parameters. The top 10 parameters resulting in the greatest changes in the deterministic ICUR are shown. UTI: urinary tract infection.

## DISCUSSION

MV140 demonstrates dominance over pAbs, with a probabilistic incremental cost-utility ratio (ICUR) of -$229 088 per additional QALY gained. MV140 represents savings in test and medical visit costs and lost productivity costs due to the increased UTI-free rate observed in patients on MV140. Furthermore, it presents a favorable safety profile, with no major safety concerns reported in comparative studies between MV140 and pAbs or in preliminary results from the first North American clinical experience study.[36] This dominance persists across multiple deterministic and

probabilistic scenario analyses, indicating that MV140 represents a cost-effective alternative to pAbs in the Canadian healthcare system. MV140 presents an important non-antibiotic prophylactic treatment option that not only exhibits efficacy after cessation of prophylactic treatment, but also prevents the development of antibiotic resistance associated with pAb therapy.[10,11,37,38] As such, the public health benefits of MV140 may extend beyond those presented in this economic model.

Some rUTI-associated aspects have been simplified in this analysis and may be considered as limitations to the model. Other assumptions include the death rate not being above the natural mortality rate, given there is negligible mortality associated with uncomplicated cystitis.[39] In terms of assumptions around frequencies of testing and costs for medical visits, this was based on authors' expert opinion. Furthermore, the impact of AEs may be underestimated. There is a possibility of patients experiencing rare, but severe allergic reactions to antibiotics requiring hospitalization, whose incidence may range from 0.1–1.7%.[40] Due to the relatively high costs associated with hospitalization, this would increase costs associated with pAb treatment. Additionally, while the base case assumes that all AEs are managed by a GP, some patients may be managed in more expensive outpatient settings, such as urgent care centers. As such, the estimate of AE costs used in the model is conservative.

A fixed duration has been used for the length of acute UTI and pyelonephritis-associated antibiotic treatment. In clinical practice, the recommended length of an antibiotic treatment course may typically range from 3-5 days, with shorter durations preferred to lower the risk of antibiotic resistance development;[17] however, the clinically plausible length of one model cycle[41] has been used for acute UTI and pyelonephritis treatment for cost calculation purposes. Furthermore, it is assumed that there is no alteration or discontinuation of prophylactic treatment in patients who do not achieve efficacy, or who experience acute UTI episodes while on prophylactic treatment; in clinical practice, prophylactic treatments may be switched if efficacy is not achieved. Therefore, treatment costs may be slightly overestimated for both MV140 and pAbs in the model.

Transition probabilities for acute UTI development used in the Markov model are derived from a retrospective study, which exhibited improvements in acute UTI rate after cessation of pAb treatment, in contrast with clinical experience.[7,9] The study was used in the base case due to its direct comparison between MV140 and pAbs and the primary outcome being directly translatable to the model;[14] however, it should be noted that the scenario with alternate transition probabilities, conducted to explore the effect of uncertainty in these parameters, also demonstrated the dominance of MV140 over pAbs in this setting.

The community setting scenario is of particular interest, as prescriptive authority for the treatment of uUTI has recently been legislated in Ontario, as it has been in several other provinces across Canada.[42,43] While the community setting scenario reflects a relatively small percentage of patients (5%) using community pharmacist services rather than a GP or urologist for acute UTI, the proportion of patients seeing community pharmacists may rise to up to 25% as awareness and utilization of this resource increases.[3] As such, costs associated with acute UTI may decrease slightly in upcoming years; however, as demonstrated in the community setting scenario, MV140 will still provide a consistently cost-effective alternative to pAbs.

## CONCLUSIONS

MV140 provides cost savings and QALY improvements over pAbs across the 1.25-year time horizon of the model and has a favorable safety profile. As such, MV140 is expected to result in considerable added value for adult female rUTI patients based on the body of clinical evidence and economic value demonstrated from the pharmacoeconomic modeling.

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