Journal of Pediatric Urology (2015) 11, 247.e1–247.e8

Economic analysis of continuous antibiotic prophylaxis for prevention of urinary tract infections in infants with high-grade hydronephrosis

H.Y.V. Tu [a,b,1], J. Pemberton [c,d,1], A.J. Lorenzo [e], L.H. Braga [a,b,c,d]

[a]Division of Urology, St. Josephs Healthcare, Institute of Urology, 50 Charlton Avenue East, Room G344, Hamilton, Ontario, L8N 4A6, Canada

[b]Division of Urology, Department of Surgery, McMaster University, 1280 Main Street West, Hamilton, Ontario, L8S 4L8, Canada

[c]McMaster Pediatric Surgery Research Collaborative, Department of Surgery, McMaster University, 1280 Main Street West, Hamilton, Ontario, L8S 4L8, Canada

[d]Department of Clinical Epidemiology and Biostatistics, McMaster University, 1280 Main Street West, Hamilton, Ontario, L8S 4L8, Canada

[e]Division of Urology – Main Office, Main Floor Black Wing Room M299, The Hospital for Sick Children, University of Toronto, 555 University Avenue, Toronto, Ontario, M5G 1X8, Canada

Correspondence to: L.H. Braga, McMaster Children's Hospital, Dept. of Surgery/Urology, McMaster University 1280 Main Street West, Hamilton, Ontario, L8S 4K1, Canada, Tel.: +1 905 521 2100x73654; fax: +1 905 570 8971

braga@mcmaster.ca (L.H. Braga)

Keywords
Hydronephrosis; Urinary tract infection; Antibiotic prophylaxis; Cost-effectiveness analysis

Received 10 September 2014
Accepted 15 April 2015
Available online 20 June 2015

Summary

Background
For infants with hydronephrosis, continuous antibiotic prophylaxis (CAP) may reduce urinary tract infections (UTIs); however, its value remains controversial. Recent studies have suggested that neonates with severe obstructive hydronephrosis are at an increased risk of UTIs, and support the use of CAP. Other studies have demonstrated the negligible risk for UTIs in the setting of suspected ureteropelvic junction obstruction and have highlighted the limited role of CAP in hydronephrosis. Furthermore, economic studies in this patient population have been sparse.

Objective
This study aimed to evaluate whether the use of CAP is an efficient expenditure for preventing UTIs in children with high-grade hydronephrosis within the first 2 years of life.

Study design
A decision model was used to estimate expected costs, clinical outcomes and quality-adjusted life years (QALYs) of CAP versus no CAP (Fig. 1). Cost data were collected from provincial databases and converted to 2013 Canadian dollars (CAD). Estimates of risks and health utility values were extracted from published literature. The analysis was performed over a time horizon of 2 years. One-way and probabilistic sensitivity analyses were carried out to assess uncertainty and robustness.

Results
Overall, CAP use was less costly and provided a minimal increase in health utility when compared to no CAP (Table). The mean cost over two years for CAP and no CAP was CAD$1571.19 and CAD$1956.44, respectively. The use of CAP reduced outpatient-managed UTIs by 0.21 infections and UTIs requiring hospitalization by 0.04 infections over 2 years. Cost-utility analysis revealed an increase of 0.0001 QALYs/year when using CAP. The CAP arm exhibited strong dominance over no CAP in all sensitivity analyses and across all willingness-to-pay thresholds.

Discussion
The use of CAP exhibited strong dominance in the economic evaluation, despite a small gain of 0.0001 QALYs/year. Whether this slight gain is clinically significant remains to be determined. However, small QALY gains have been reported in other pediatric economic evaluations. Strengths of this study included the use of data from a recent systematic review and meta-analysis, in addition to a comprehensive probabilistic sensitivity analysis. Limitations of this study included the use of estimates for UTI probabilities in the second year of life and health utility values, given that they were lacking in the literature. Spontaneous resolution of hydronephrosis and surgical management were also not implemented in this model.

Conclusion
To prevent UTIs within the first 2 years of life in infants with high-grade hydronephrosis, this probabilistic model has shown that CAP use is a prudent expenditure of healthcare resources when compared to no CAP.

[1] Both authors contributed equally to the preparation of the manuscript.

http://dx.doi.org/10.1016/j.jpurol.2015.04.031

Table Base case results.

Treatment arm	Expected value			
	Cost (CAD$)	Number of UTIs	Number of inpatient UTIs	Quality-adjusted life years
Continuous antibiotic prophylaxis	1571.19	0.204	0.010	1.6986
No continuous antibiotic prophylaxis	1956.44	0.418	0.049	1.6985
Incremental (continuous antibiotic prophylaxis − no continuous antibiotic prophylaxis)	−385.25	−0.213	−0.039	0.0001

Introduction

Despite the paucity of high-level evidence-based data, continuous antibiotic prophylaxis (CAP) continues to be empirically recommended in order to reduce the UTI rate in infants, particularly in the first 2 years of life [1]. The rationale for this approach is based on reported incidences of febrile UTIs in children with hydronephrosis (HN); incidences range between 4 and 50%, depending on the etiology [2]. Recent evidence suggests that neonates with obstructive uropathy and severe HN are at an increased risk of UTI, which supports the concept that CAP should be given to this population [2–4]. Conversely, other studies have reported a negligible risk of UTI in patients with suspected ureteropelvic junction obstruction (UPJO) and that CAP offers little or no benefit; thus, antibiotics should no longer be recommended, regardless of severity of HN [5–7]. Given this evident clinical equipoise, a high-quality randomized controlled trial (RCT) is currently being conducted to provide definitive treatment recommendations [8]. However, treatment efficacy derived from RCTs only comprises part of a patient-care-improvement strategy, as additional information such as economic evaluations is typically required prior to health policy implementation.

Few economic studies have been conducted in pediatric urology, with the majority of the existing literature surrounding the assessment of surgical interventions [9]. It is believed that there are no reports, to date, of economic evidence for the use of CAP (versus no treatment) to prevent UTIs in infants with HN within the first 2 years of life. With this in mind, data were extracted from a recent systematic review [10] to inform a probabilistic decision model analysis, with the goal of systematically evaluating whether offering CAP to children with high-grade HN within the first 2 years of life, for prevention of febrile UTIs, is an efficient use of limited Canadian healthcare resources.

Materials and methods

A probabilistic decision model was developed to estimate expected costs, clinical outcomes and quality-adjusted life years (QALYs) of two treatment options commonly offered to infants with high-grade HN: (1) CAP and (2) expectant management (i.e. no CAP). The base case consisted of an infant with Society of Fetal Urology (SFU) Grade III or IV HN, without VUR and with an anterior posterior diameter (APD) of the renal pelvis $\geq$15 mm. The analysis was performed from a third party payer perspective with a time horizon of 2 years, as this is the current recommendation for CAP duration in this patient population [11]. This study used discounting − the process of adjusting the value of future costs and benefits to allow for their comparison with present day data [12]. A discount rate of 5% was performed on all year-2 costs and consequences according to consensus recommendations [13].

Model design

The decision tree included two 1-year phases (Fig. 1) using the base case as described above. Treatment options at the decision node included either CAP or no CAP. Regardless of treatment status, each base-case infant entered one of three health states of 1-year duration per cycle: well with no UTIs, occurrence of an outpatient-managed UTI (UTI_o), or occurrence of an inpatient-managed UTI (UTI_i). The proportion of patients developing UTI_o and UTI_i differed between treatment groups, and the pathways were mutually exclusive and exhaustive. This model estimated the expected costs of being in each of the three states described above, as well as the expected number of UTIs and expected QALYs for both treatment groups.

Calculation of Incremental Cost Effectiveness Ratios (ICERs) was planned in case of lack of dominance of a treatment group on the three health states.

Model assumptions

It was assumed that in this model, no early resolution or downgrading of HN occurred (i.e. patient's HN did not decrease from high grade (SFU III/IV) to low grade (SFU I/II), or resolved completely). If a patient's HN either decreased or resolved, CAP would no longer be indicated. The next assumption was that all patients in the CAP group had 100% compliance with their medication. This assumption was derived from the current patient medication compliance of the pilot randomized controlled trial on antenatal hydronephrosis (ALPHA), which was 98% [8]. It is believed that, to date, there is no accurate data regarding the compliance rate to CAP in the pediatric population; thus, an assumption had to be made regarding compliance rates. A further assumption was that the risk of surgical intervention did not differ between treatment groups, and that no patients from either group required surgery during the first 2 years of life. Current literature on rates of surgery in the high-grade HN population reflected no differences based on CAP status [3]. Finally, the last assumption was that the probability of developing a UTI in year 2 was

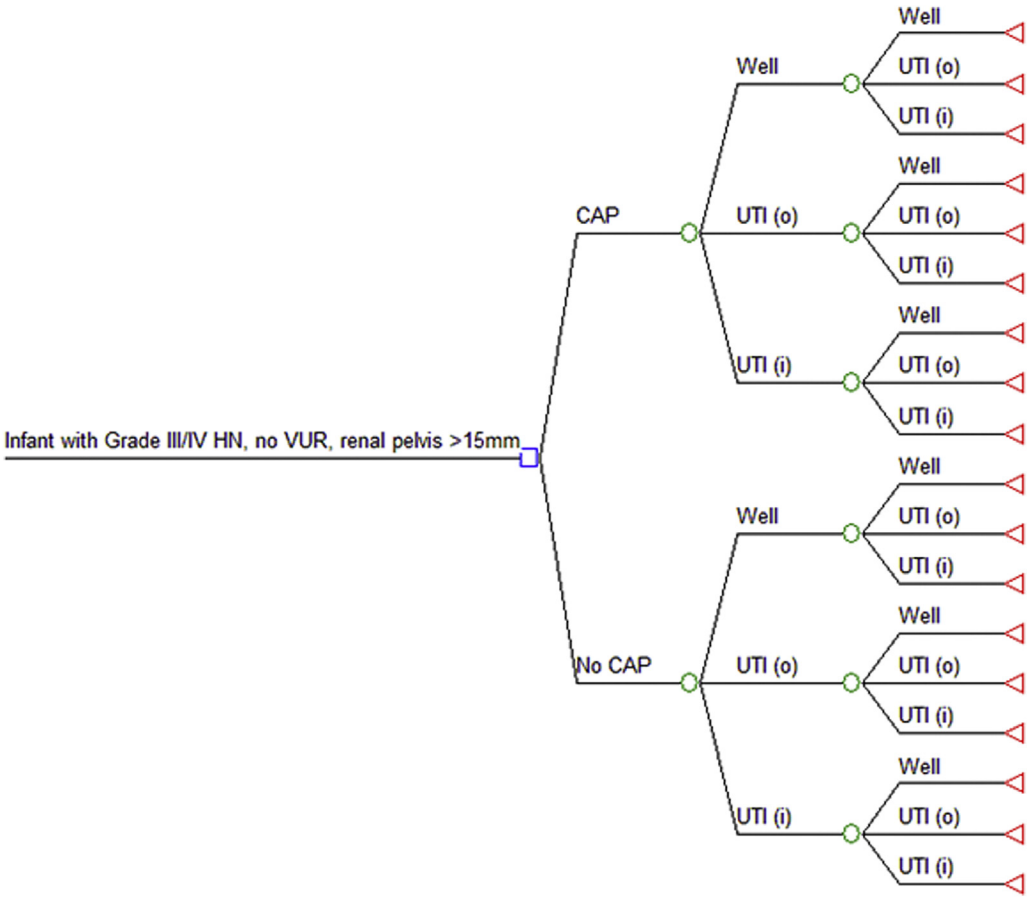

Figure 1 Structure of decision model. Abbreviations: CAP (continuous antibiotic prophylaxis), HN (hydronephrosis), UTI(o) (outpatient-managed urinary tract infection), UTI(i) (inpatient-managed urinary tract infection), VUR (vesico-ureteral reflux).

independent of the patient's UTI status in year 1. This is due to the lack of high-quality UTI probability estimates in the second year of life in the literature.

Outcome measures

Three different outcomes were assessed: two measures of effectiveness and one of health utility.

Effectiveness measures

1. Overall number of UTIs over 2 years

This was a dichotomous outcome where the patient either developed a UTI or did not within each 1-year phase. This outcome did not differentiate between UTI_o and UTI_i. For each potential pathway, a patient could either develop zero, one or two UTIs over the 2-year time horizon. For this outcome, a lower score represented a lower number of UTIs.

2. Number of UTIs that required hospital admission over 2 years

This was also a dichotomous outcome where the patient either developed a UTI_i or did not within each 1-year phase. UTI_i was intended to capture a more severe UTI that required hospital admission and, thus, represented a more costly outcome. Each potential pathway resulted in either no UTI_i, one or two UTI_i over the 2-year time horizon.

Utility measure

3. Quality-adjusted life years

A health utility value was assigned to each of the three potential health states (well, UTI_o and UTI_i) from values published in the literature. An estimated duration for each health state was obtained from a panel of pediatric urologist clinical experts and informed by enrolled patients in the ALPHA trial [8]. These values were combined to obtain expected QALYs for each potential pathway. For this outcome, a higher score represented the QALYs gained for a given pathway.

Determining model probabilities (Appendix 1)

A recent systematic review was examined in order to determine reliable probabilities of UTI rates for HN patients on CAP versus those not on CAP [10]. Twenty-one studies were selected and pooled rates of UTI from 3876 patients were analyzed. The meta-analysis demonstrated that in patients with high-grade (III/IV) HN, a significant decrease

in UTI rates was observed in those receiving CAP versus those not on CAP (14.6% vs. 28.9%, $P < 0.01$).

In order to determine hospitalization rates for patients with a febrile UTI, Walsh and colleagues [14] investigated the risk of hospital admissions for infants with pyelonephritis with and without HN. The overall hospitalization rate for patients with HN was reported as 5% (26/522); however, the study did not stratify this rate by HN severity [14]. According to another trial, the hospitalization due to UTI was 8% in the CAP group versus 10% in the placebo group [15]. Finally, a prospective cohort study that followed 192 patients diagnosed with renal pelvic dilation with a median follow-up of 24 months (interquartile range 12—39) was identified. All patients were prescribed CAP at birth and the Kaplan—Meier survival curves revealed a UTI cumulative incidence of 8% at 12 months and 13% at 24 months [16].

Determining treatment costs (Appendix 2)

Costs for each of the three health states (well, UTI_o and UTI_i) were separately calculated, prior to being combined in the decision model. For the well health state, costs were derived from the Ministry of Health and Long-term Care Schedule of Benefits for Physician Services (MOHLTC SOB) [17] and included an initial consultation visit with a pediatric urologist and a renal bladder ultrasound. In the first year, additional costs included the 3-, 6-, 9-, and 12-month follow-up visits, with each clinic visit being associated with a mandatory renal bladder ultrasound, according to the clinical protocol. Overhead costs were not included as these costs were consistent between treatment groups regardless of medication status. In the second year, a similar number of follow-up clinic visits and renal bladder ultrasounds were included. Each ultrasound consisted of both diagnostic and technician fees.

Additional medication-associated costs were collected for both the CAP treatment group and for the oral antibiotics needed to treat a UTI_o. These included the medication cost for a standard dose obtained from the Ontario Drug Benefit (ODB) Formulary [18], which was then combined with the dose and frequency recommendations for trimethoprim/sulfamethoxazole (TMP / SMX) (DIN 00726540) from the American Academy of Pediatrics (AAP) and using standardized weight curves by age [1]. TMP/SMX has been recommended by the AAP as the gold standard for CAP and therapeutic treatment in this patient population. Therefore, it was used in this study despite other medications being used in the clinical setting. In addition, mark-up costs were added for both the ODB (8%) and pharmacy (10%). Detailed calculations can be found in Appendix 3.

In addition to the medication needed to treat a UTI_o, several other expenses were considered. For this calculation, it was assumed that the patient was first seen at their local pediatrician or family physician, had a bag urinalysis and urine dipstick positive for nitrites and leukocytes. Following a positive urine dipstick, the patient was then sent to a tertiary hospital and seen in the Emergency Room (ER). At the ER, the child was catheterized and a urine-specimen was taken and sent for culture. This assumed care pathway, derived from the ALPHA trial [8], was intended to obtain a true documented UTI and mitigate the effects of over treating false-positive UTIs diagnosed from bagged specimens. All costs were adjusted to 2013 Canadian dollars (CAD) using the Bank of Canada's inflation calculator [19].

Finally, costs associated with a UTI_i were obtained from the Ontario Case Costing Initiative (OCCI) [20] and again corrected to 2013 CAD. Within the OCCI cost estimate, a mean length of stay of 5.7 days was used, and indirect and direct costs based on average of 80 admissions from all participating hospitals were included in the UTI_i costing estimate.

Determining utilities

Quality-adjusted life years

Quality-adjusted life years and expected QALYs were calculated for each pathway contained within the decision model (Table 1). First, health utility values were obtained using close estimates from predetermined values published in the literature and the Cost Effectiveness Analysis Registry from Tufts Medical Center [21]. A health utility value of 0.87 for VUR was used [22] as no utility value for HN has been established thus far [21]. Existing utility values were found for UPJO [23]; however, unlike the VUR estimates, these utilities were not based on a direct estimation study using standardized economic evaluation techniques. These UPJO utilities were used to inform the sensitivity analysis but were not used in the base-case analysis for the aforementioned reasons. It is believed that, to date, a utility value for the combined health state of hydronephrosis, outpatient and inpatient UTI has not been reported. An approximation was created through the multiplication of the VUR utility and available utility values (approximation factor for UTI) for non-systemic infection (pneumonia) and severe bacteremia for UTI_o and UTI_i, respectively. Included in this calculation was the assumption that when not

Table 1 Base case quality-adjusted life years calculations.

Health state	Utility value[a]	Approximation for UTI	Duration in health state (years)	Quality-adjusted life years[b]	Source
Well	0.87		1	0.87	Lloyd et al. [22]
UTI_o	0.865	0.994	0.019231	0.8699	
UTI_i	0.832	0.957	0.038462	0.8686	

Abbreviations: UTIo (outpatient-managed urinary tract infection), UTIi (inpatient-managed urinary tract infection).

[a] Calculated as Utility value in well state* approximation for UTI.

[b] Calculated as. Σ*Utility value in health state* $*$ *Duration in health state*

experiencing a UTI, the patient's utility returned to the baseline 'well health state' utility for the remaining duration of the year in each phase.

Further calculations were necessary to transform the health utility values into QALYs. First, the duration of each utility value needed to be established. Based on previous experience with patients enrolled in the ALPHA trial who developed a UTI, the duration for UTI_o was 1 week and for UTI_i it was 2 weeks. This estimated duration included the onset of symptoms until resolution and completion of prescribed antibiotics. In order to improve clinical accuracy, the duration of UTIs was factored into the QALY calculation. Using methods described by Drummond et al. [12], overall QALYs for a UTI health state were calculated by adding the QALYs associated with a UTI to the QALYs gained from being infection free.

Determining willingness-to-pay threshold

A willingness-to-pay (WTP) threshold of US$50,000 (1982) per QALY was used in the base case analysis to determine whether an intervention was cost-effective, as defined in previous value-of-life literature [24]. Using the United States Consumer Price Index [25] to adjust for inflation, at the time of writing the WTP threshold in 2013 CAD was approximately CAD$130,000 per QALY. In comparison with the Canadian healthcare system, a recent paper published by the University of Toronto Health Economics department (UTMH 2013) quoted a WTP range of CAD$20,000 to CAD$100,000 per QALY in 1992. Adjusting for inflation using the Canadian Consumer Price Index [25], the WTP range is equivalent to CAD$29,000 to CAD$145,000 (2013) per QALY. Thus, the WTP threshold as derived from the US healthcare system is applicable to this model, as it falls within the accepted WTP ranges described for the Canadian healthcare system.

One-way and probabilistic sensitivity analyses

One-way sensitivity (OWS) analyses were performed to assess the impact of a number of structural assumptions and alternative patient characteristics on the model results. All model parameters utilized in the one-way sensitivity analysis are outlined in Appendix 1. Confidence intervals around a point estimate were used from published meta-analysis, where possible. If not possible, efforts were made to make an informed estimate based on reported measures of variance (i.e. standard deviations). For costing estimates, 95% CI around the standard deviation for inpatient hospitalization costs were obtained from OCCI. Due to the nature in which the other costs were obtained, only costs for inpatient hospitalizations were included in the sensitivity analysis. Finally, a probabilistic sensitivity analysis was conducted to ensure all possibilities were exhaustively explored across all willingness-to-pay thresholds. All analyses were conducted using TreeAge software (Williamston, Massachusetts).

Results

Base case: Overall, the estimated expected costs for CAP use for prevention of UTIs in infants with high-grade HN were CAD$1571.19 versus CAD$1956.44 when CAP was not utilized. Use of CAP was estimated to reduce costs by CAD$385.25, UTI_o by 0.21 infections and UTI_i by 0.04 infections, as well as to produce 0.0001 more QALYs when compared to no CAP (Table 2). The use of CAP exhibited strong dominance over not using CAP, as it was less costly, more effective in reducing UTIs and increasing QALYs; therefore, an incremental cost effectiveness ratio was not calculated.

Sensitivity analysis: Many different parameters were varied according to literature-derived ranges and their effect on the two clinical outcomes and QALYs graphically illustrated (Appendix 4). A WTP threshold of CAD$130,000 per QALY was used as defined previously for the base case and one-way sensitivity analysis (Fig. 2). Probabilistic sensitivity analysis was performed and demonstrated that CAP use continued to exhibit strong dominance, as no overall changes were observed in the cost-effectiveness or cost-utility analysis at all willingness-to-pay thresholds (Fig. 3a and b).

Discussion

Overall, this probabilistic model provided a Canadian-specific assessment of two cost effectiveness and one cost utility measures. Across all three outcomes, CAP use was shown to be a better expenditure of scarce healthcare resources when compared to no utilization of CAP for the prevention of UTI in infants with high-grade HN.

It is important to note that from the analysis the QALYs gained per year from CAP use compared to no CAP use were quite small. Whether a gain of 0.0001 QALYs per year is clinically relevant remains to be determined. It is probably not clinically important; however, small QALY differences have also been seen in other pediatric urology economic evaluations. A study examining the use of tolterodine

Table 2 Base case results.

Treatment arm	Expected value				ICER		
	Costs (CAD$)	Number of UTIs	Number of UTI_is	QALYs	$/UTI	$/$UTI_i$	$/QALY
CAP	$1571.19	0.204	0.010	1.6986	—	—	—
No CAP	$1956.44	0.418	0.049	1.6985	—	—	—
Incremental (CAP-no CAP)	−$385.25	−0.213	−0.039	0.0001	Dominated	Dominated	Dominated

Abbreviations: CAP (continuous antibiotic prophylaxis), ICER (incremental cost-effectiveness ratio), UTI (urinary tract infection), UTIi (inpatient-managed urinary tract infection).

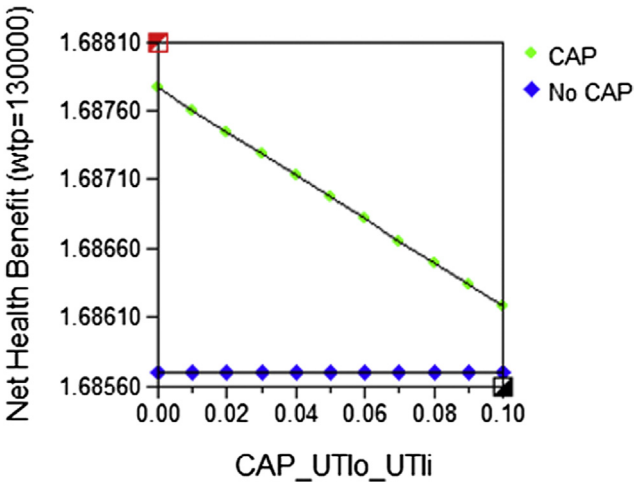

Figure 2 Sensitivity analysis of CAP-UTIo-UTIi pathway. Abbreviations: CAP (continuous antibiotic prophylaxis), CAP_UTIo_UTIi (pathway describing infant on continuous antibiotic prophylaxis with an outpatient-managed UTI in the first year of life and an inpatient-managed UTI in the second year), wtp (willingness-to-pay).

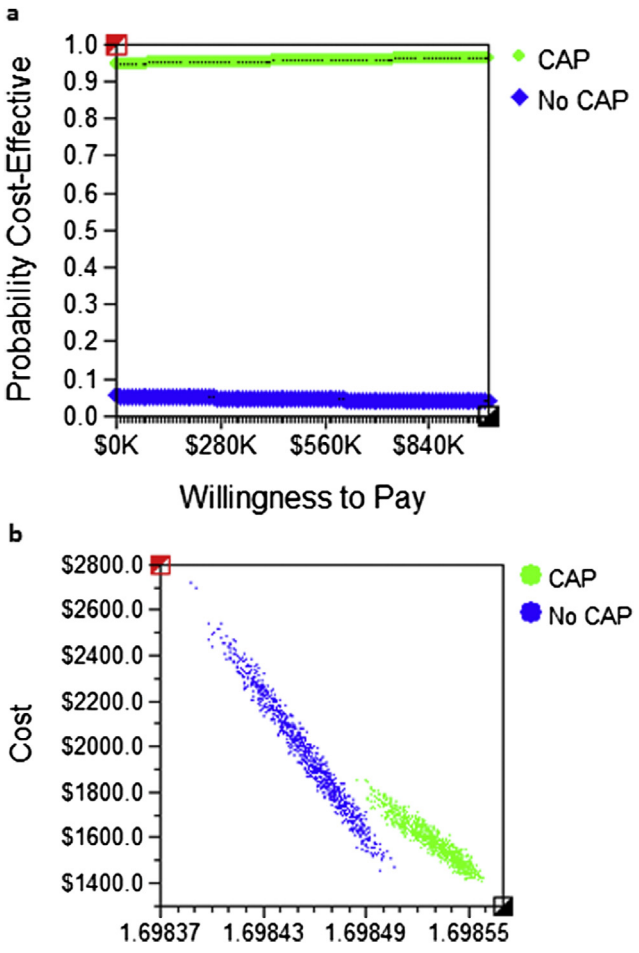

Figure 3 a. Acceptability curve of probabilistic sensitivity analysis. Willingness to pay in 2013 Canadian dollars. b. Cost-utility scatter plot of cost in 2013 Canadian dollars versus QALY.

versus no treatment for children with over-active bladder revealed only a 0.03 QALY difference between groups [25]. Overall, despite the potential lack of clinical significance, the CAP arm was still dominant, as it remained the least costly and most effective in terms of QALYs per year gained and UTIs prevented.

After general consensus among the authors, the use of a 2-year horizon was decided upon in concordance with the CUA guidelines on antenatal hydronephrosis. Similarly, the time horizon used in the AAP clinical practice guidelines for febrile UTIs [1] was also centered upon the initial 2 years of life. Justification for the choice of time horizon included a higher incidence rate of UTIs in this age group that is typically associated with more systemic infections. Furthermore, in their prospective study, Coelho et al. reported on a reduction in UTI episodes from the first to second year of life, thereby reducing the likelihood of CAP use given the lower risk of UTIs after the second year of life [16].

The limit to the maximum number of UTIs per year in the present model was chosen to mitigate the effect of recurrent UTIs on the analysis. Studies have shown that patients that are prone to recurrent UTIs also tend to have VUR. However, according to a recent study by Zareba et al. [26], only 21% of patients with antenatal hydronephrosis had VUR. Moreover, recurrent UTIs in this patient population would constitute an indication for surgical intervention, ultimately excluding these patients from the present study.

Strengths of the present study included collecting probabilities of overall UTI rates in both CAP and no CAP groups from a recent systematic review and meta-analysis, and exploring uncertainty in a comprehensive one-way and probabilistic sensitivity analysis. Other strengths of the model included high precision in estimating associated costs, converting all costs to 2013 CAD, where applicable, and the use of micro-costing, where available. The care pathway modeled in this study was informed by patients enrolled in a current RCT, which is investigating the clinical efficacy of CAP in the exact same patient population [8].

The following limitations of this study were: firstly, in the second year of life, the evidence for estimating UTI probabilities in both groups was lacking in the literature. Further high-quality evidence is needed to improve this parameter. Secondly, as it normally occurs with any cost-utility analyses in pediatric urology, the estimation of the health utility values was challenging. Direct estimation of health utility values for HN was not possible and values were instead adopted from a study investigating VUR. Although important clinical distinctions between the health states of HN and VUR exist, the only other potential option for a previously reported utility value that could be clinically equivalent to HN was from a study on UPJO. This study reported a utility value for UPJO as 0.65, which seemed very low compared to other published urological health utility values, including: ureteroscopy (0.914), extracorporeal shock wave lithotripsy (0.967) and chronic urolithiasis (0.974) [27]. For pediatric urological conditions, it is recognized that the derivation of direct health utility values are challenging, resulting in a wide variety of health utility values utilized in this cost-effectiveness analysis. Even though a recent economic analysis has identified new utility values for VUR [22], further studies are required for direct estimation of health utility values for HN, which

would be a valuable contribution to pediatric literature. Thirdly, while gender, circumcision status and etiology of HN may interfere with UTI rates, a generic case of high-grade HN without VUR was adopted to be the clinical scenario for the decision model analysis. It is believed that having a broad, common base case simplified the analysis and allowed for more generalizability of the results.

Further limitations in this study included a lack of comparison of the results of the present study with the existing literature due to the lack of medication-based economic evaluations in pediatric urology, as most existing studies were focused on surgical interventions, as well as the assumption regarding absence of HN resolution or potential surgical management. These assumptions do not reflect the natural course of HN patients, as it is known that two thirds of high-grade HN patients resolve within 24 months to either SFU Grade I or II. However, due to the nature of a decision tree model, these factors could not be incorporated in the model. It is recognized that the assumption of 100% antibiotic compliance might be too optimistic, but this data was derived from a pilot randomized trial results [8]. As a future direction, upon the completion of a current RCT on antenatal HN, we hope to populate a Markov model and determine whether such a model would create a more accurate representation of the patient population. Nonetheless, overall, the base case used in the present study does represent most high-grade HN patients and, therefore, is still an important first step. Finally, it would be interesting to incorporate societal costs into the analysis such as caregiver hours of lost productivity for emergency department visits or hospital admissions. This would increase the applicability of the results in healthcare policy making. Further work needs to be done on collecting the impact of HN, regardless of treatment, on caregiver productivity loss, follow-up visitation costs, and societal costs for both UTI_o and UTI_i health states [28].

Conclusion

Overall, this probabilistic model provided a Canadian-specific assessment of two cost effectiveness and one cost utility measure. Using CAP was found to be a better expenditure of healthcare resources when compared to not using CAP for prevention of UTI in infants with high-grade HN within the first 2 years of life. The results of this economic evaluation should be combined with findings from a RCT on effectiveness of CAP for the prevention of UTI in HN patients prior to providing definitive health policy recommendations on this matter.

Conflict of interest statement

All authors have no conflicts to disclose.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpurol.2015.04.031.

References

[1] American Academy of Pediatrics. Committee on quality improvement. Subcommittee on urinary tract infection. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. Pediatrics 1999;103:843—52.

[2] Song SH, Lee SB, Park YS, Kim KS. Is antibiotic prophylaxis necessary in infants with obstructive hydronephrosis? J Urol 2007;177:1098—101.

[3] Williams G, Craig J. Antibiotics for the prevention of urinary tract infection in children: a systemic review of randomized controlled trials. J Pediatr 2001;138:868—74.

[4] Ditchfield MR, Grimwood K, Cook DJ, Powell HR, Sloane R, Nolan TM, et al. Time course of transient cortical scintigraphic defects associated with acute pyelonephritis. Pediatr Radiol 2002;32:849—52.

[5] Islek A, Guven AG, Koyun M, Akman S, Alimoglu E. Probability of urinary tract infection in infants with ureteropelvic junction obstruction: is antibacterial prophylaxis really needed? Pediatr Nephrol 2011;26:1837—41.

[6] Lin KY, Chiu NT, Chen MJ, Lai CH, Huang JJ, Wang YT, et al. Acute pyelonephritis and sequelae of renal scar in pediatric first febrile urinary tract infection. Pediatr Nephrol 2003;18:362—5.

[7] Benador D. Are younger children at highest risk of renal sequelae after pyelonephritis? Lancet 1997;349:17—9.

[8] Braga LH, Pemberton J, Heaman J, Demaria J, Lorenzo AJ. Pilot randomized, placebo controlled trial to investigate the effect of antibiotic prophylaxis on the rate of urinary tract infection in infants with prenatal hydronephrosis. J Urol 2014 May;191:1501—7.

[9] Hsieh MH, Meng MV, Baskins LS. Outcomes and cost analysis of pyeloplasty for antenatally diagnosed UPJO using Markov models. Urology 2008;72:794—9.

[10] Braga LH, Mijovic H, Farrokhyar F, Pemberton J, DeMaria J, Lorenzo A. Antibiotic prophylaxis for urinary tract infections in antenatal hydronephrosis. Pediatrics 2013;131:e251—61.

[11] Psooy K. Investigation and management of antenatally detected hydronephrosis. Can Urol Assoc J 2009;3:69—72.

[12] Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. 4th ed. Oxford UK: Oxford University Press; 2005.

[13] Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analysis. Panel on cost-effectiveness in health and medicine. JAMA 1996;276:1339—41.

[14] Walsh TJ, Hsieh S, Grady R, Mueller BA. Antenatal hydronephrosis and the risk of pyelonephritis hospitalization during the first year of life. Urology 2007;69:970—4.

[15] Craig JC, Simpson JM, William GJ, Lowe A, Reynolds GJ, McTaggart SJ, et al. Antibiotic prophylaxis and recurrent urinary tract infection in children. N Engl J Med 2009;361:1748—59.

[16] Coelho GM, Bouzada MC, Lemos GS, Pereira AK, Lima BP, Oliveira EA. Risk factors for urinary tract infection in children with prenatal renal pelvic dilatation. J Urol 2008;179:18—9.

[17] Schedule of benefits for services under the health insurance act [Internet]. Ontario: Ministry of Health and Long-term Care; c 2002 [updated 2014 Jan 05; cited 2014 April 9] Available from: http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html [accessed 26.06.15].

[18] Ontario drug benefit formulary [Internet]. Ontario: Ministry of Health and Long term Care; c 2008 [updated 2014 Jan 16; cited 2014 April 13]. Available from: http://www.health.gov.on.ca/en/public/programs/drugs/programs/odb/odb.aspx [accessed 26.06.15].

[19] Inflation Calculator [Internet]. Bank of Canada. [cited 2014 April 13]. Available from: http://www.bankofcanada.ca/rates/related/inflation-calculator/ [accessed 26.06.15].
[20] Ontario case costing initiative [Internet]. Ontario: Ministry of Health and Long term Care. [updated 2013 April; cited 2014 Jan 05]. Available from: http://www.occp.com/mainPage.htm [accessed 26.06.15].
[21] Cost-effectiveness analysis registry [Internet]. Tufts medical Center.c 2007—2013 [cited 2013 April 09]. Available from: https://research.tufts- nemc.org/cear4/ [accessed 26.06.15].
[22] Lloyd JC, Yen T, Pietrobon R, Wiener JS, Ross SS, Kokorowski PJ, et al. Estimating utility values for vesicoureteral reflux in the general public using an online tool. J Ped Urol 2014;10:1026—31.
[23] Mesrobian HG. The value of newborn urinary proteome analysis in the evaluation and management of ureteropelvic junction obstruction: a cost-effectiveness study. World J Urol 2009;27:379—83.
[24] King Jr JT, Tsevat J, Lave JR, Roberts MS. Willingness to pay for a quality-adjusted life year: implications for societal health care resource allocation. Med Decis Mak 2005;25:667—77.
[25] Consumer Price Index Inflation Calculator [Internet]. Washington: United States Bureau of Labor Statistics. [cited 2014 Jan 11]. Available from: http://www.bls.gov/data/inflation_calculator.htm [accessed 26.06.15].
[26] Zareba P, Lorenzo AJ, Braga LH. Risk factors for febrile urinary tract infection in infants with prenatal hydronephrosis: comprehensive single center analysis. J Urol 2014;191:1614—8.
[27] Fann CY, Huang PO, Yen AM, Chen HH. Patient utility measurement for managing ureteral stones: a modified standard gamble approach. Value Health 2012;1:87—92.
[28] Kokorowski PJ, Routh JC, Nelson CP. Quality assessment of economic analyses in pediatric urology. Urology 2013;81:263—7.