Economic Consequences of Preventable Bladder Tumor Recurrences in Non-Muscle Invasive Bladder Cancer Cheryl Lee, MD¹; Denise Globe, PhD²; Danielle Colayco, PharmD, MS²; Amanda Gilmore, PhD, MPH³; Thomas Bramley, RPh, PhD³ ¹University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; ²Allergan, Inc., Irvine, CA; ³Xcenda LLC, Palm Harbor, FL

ABSTRACT

OBJECTIVES: In 2010, an estimated 70,500 new cases of bladder cancer will be diagnosed in the United States (US); 70% will present as non-muscle invasive bladder cancer (NMIBC). The instillation of intravesical chemotherapy after transurethral resection of bladder tumor (TURBT) can reduce the risk of tumor recurrence. The objective of this study is to estimate the economic consequences associated with unnecessary recurrences in patients deprived of perioperative chemotherapy (PC).

METHODS: A decision-tree model estimated the economic consequences of recurrence in patients not receiving PC. Two sources were used to estimate rates for the model because neither data source had both of the rates required; 1,010 NMIBC patient charts (from 259 US urologists) estimated therapy utilization, and recurrence rates were obtained from 502 patients enrolled in a trial by Tolley, et al randomizing patients to mitomycin C (MMC) vs no PC. Costs were estimated using prevailing Medicare reimbursement rates for TURBT (\$1,982), Bacillus Calmette-Guérin (BCG) induction therapy (\$201 / instillation), MMC induction therapy (\$252 / instillation) and perioperative MMC (\$166 / instillation).

RESULTS: Within the cohort, 17% of patients received PC after the initial TURBT. The overall recurrence rate was 39%. At first recurrence, 27% received PC and 48.6% received induction therapy with BCG (85%) or MMC (15%). Data from the randomized trial indicate that at 2 years, 36% of patients receiving PC recur compared with 53% receiving TURBT alone. Population estimates predict 49,350 new cases of NMIBC in the US in 2010. The model demonstrated prevention of 6,962 bladder recurrences with perioperative MMC after initial TURBT, with an estimated savings of \$2,608 per patient. This translates into aggregate savings of \$18.1 million to the US healthcare system over two years.

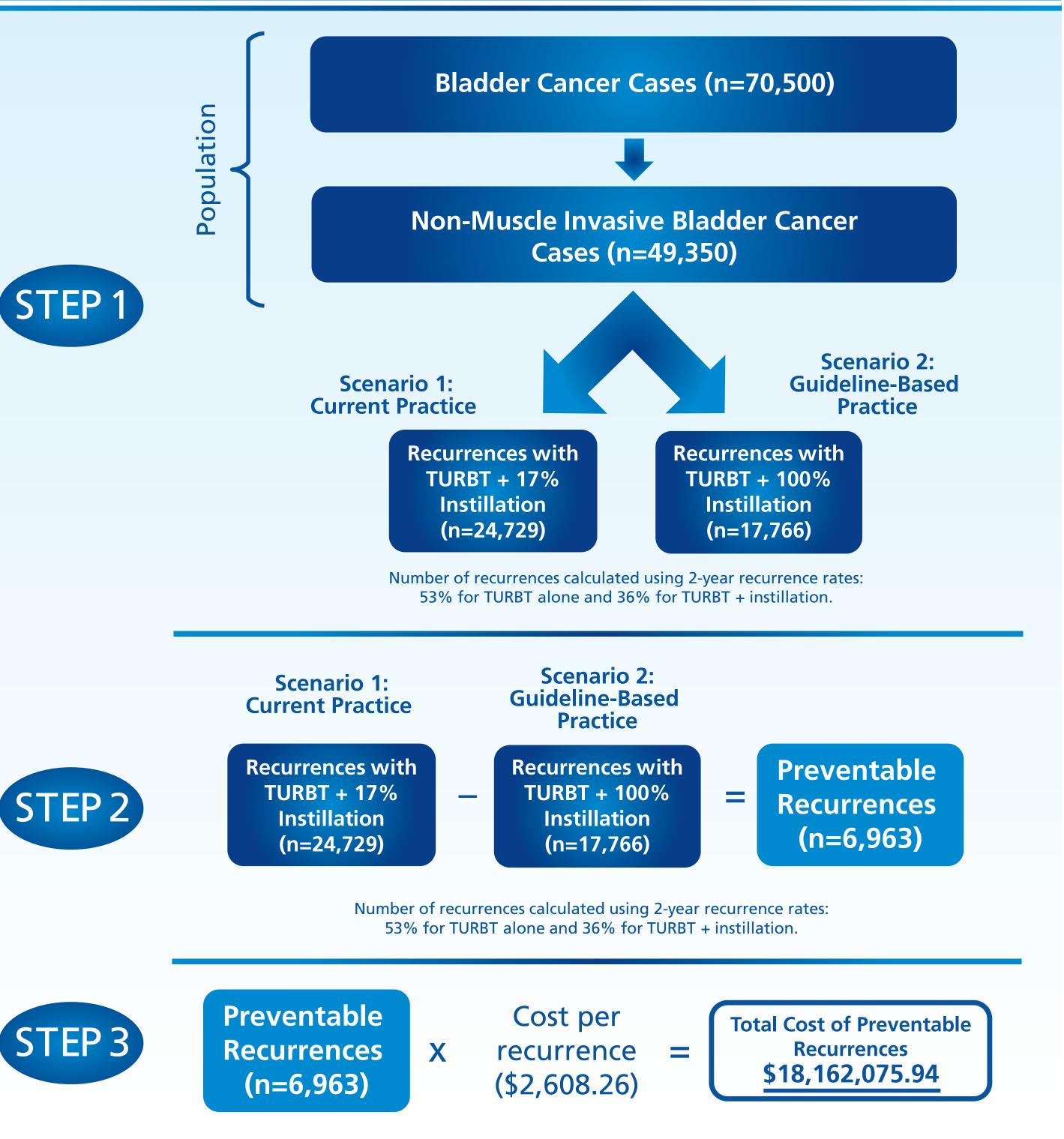
CONCLUSIONS: Greater use of PC after TURBT can reduce economic loss related to preventable bladder tumor recurrences with substantial savings to the healthcare system.

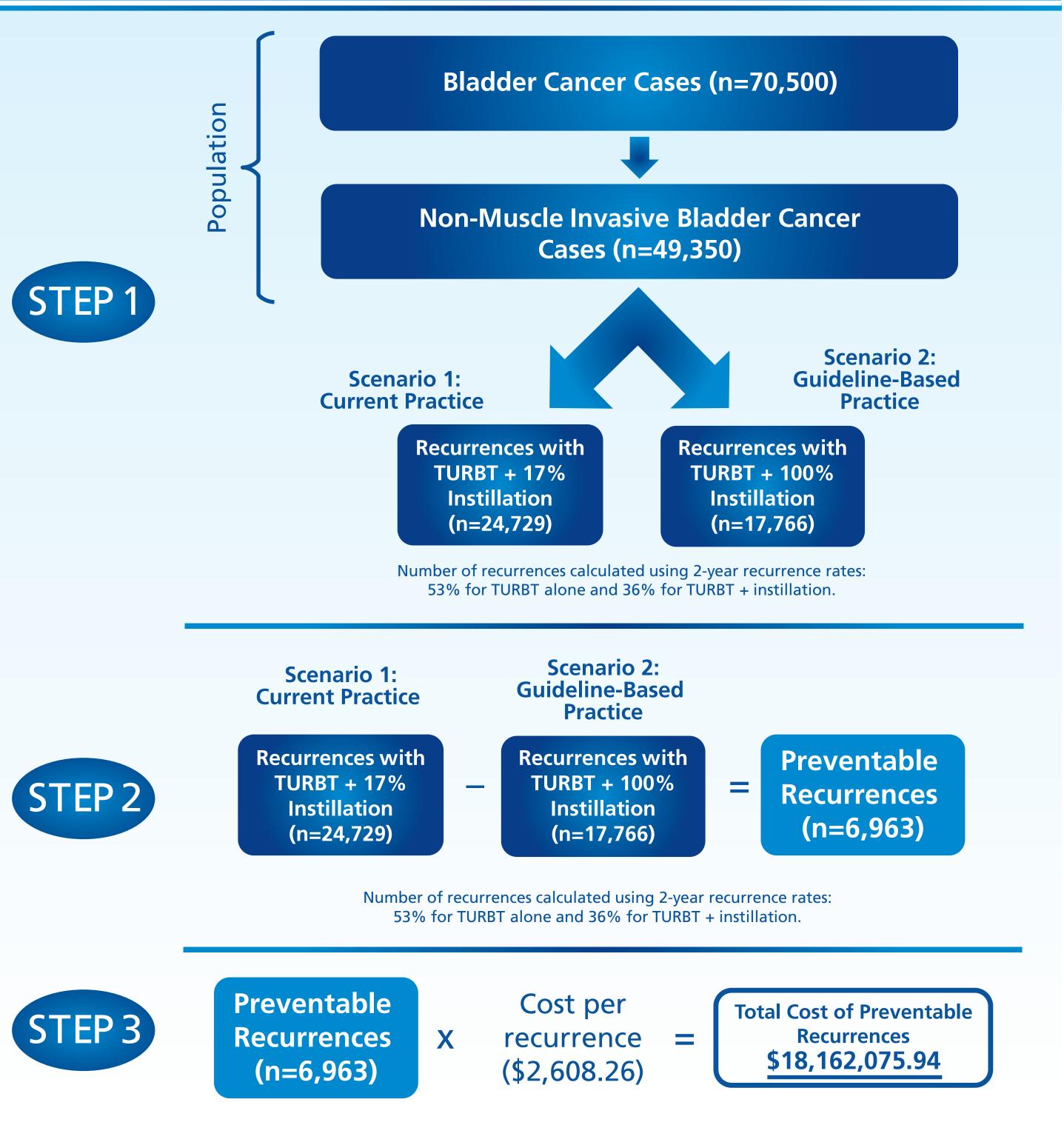
BACKGROUND

- Bladder cancer is one of the most common malignancies in the US, with an estimated 70,530 new cases and a projected 14,680 deaths in 2010 (Jemal 2010). The estimated prevalence of bladder cancer was 535,236 individuals in 2007 (Altekruse 2010).
- Approximately 70% of newly diagnosed cases of bladder cancer are non-muscle invasive (Pashos 2002).
- Bladder cancer is the ninth most costly cancer in the US and was estimated to cost \$3.5 billion in 2006 (NCI 2010).
- It has been reported that bladder cancer has the highest lifetime treatment costs per patient of all cancers, due to its high recurrence rate, low mortality rate, and costs associated with disease surveillance and treatment (Botteman 2003, Sievert 2009).
- Per patient lifetime bladder cancer costs were estimated to range from \$96,000 to \$187,000 in 2001 US dollars (Botteman 2003).

 Treatment guidelines recommend adjuvant intravesical chemotherapy for NMIBC patients to reduce the risk of tumor recurrence (Nieder 2005, AUA 2007, Babjuk 2009). However, the use of immediate intravesical chemotherapy remains inappropriately low, with estimates ranging from 0.33% to 27% (Madeb 2009, NCI 2010). This may result in a substantial number of preventable NMIBC recurrences and, thus, have significant economic implications.

recurrences.





OBJECTIVES

This study sought to develop a decision analytic model to estimate the economic burden associated with these preventable bladder tumor

METHODS

Model Overview

• A decision analytic single cycle model was built using Microsoft Excel 2007 software to estimate the costs associated with preventable bladder cancer recurrences (Figure 1).

• The perspective adopted was that of the US health care system and included direct medical costs; no direct non-medical costs or indirect costs were included.

• The time horizon of two years was utilized, and discounting was not applied.



Population At-Risk

• An estimated 70,500 new cases of bladder cancer was multiplied of 49,000 cases of NMIBC.

Preventable Recurrences

- intravesical chemotherapy was 17% (Cookson 2011).
- Recurrence rates were obtained from a 502-patient trial.
- after TURBT (Cookson 2011).

Table 1: Model population parameters

Parameter

Bladder cancer cases (#)

NMIBC (%)

Not receiving post-operative instillation (%)

Recurrence rate for TURBT alone

Recurrence rate for TURBT plus immediate intravesical chemotherapy

Cost Estimate of Preventable Recurrences

- According to the chart review, 27% of patients with a recurrence BCG induction; and 7% of patients received MMC induction.
- It was assumed that 100% of patients with a recurrence would receive a TURBT.
- It was assumed that on average, patients with a recurrence would receive a total of 6 instillations for induction.
- (HOPPS, CMS).

Table 2: Treatment cost parameters

Parameter
TURBT
Single instillation of MMC
BCG induction (per instillation
MMC induction (per instillatio

by 70% (Witjes 2008) to obtain an estimated annual incidence

• Based on a chart review study of 1,010 NMIBC patients (from 259 US urologists) the estimated utilization rate of post-TURBT

• The recurrence rate for TURBT alone was 53% versus 36% for TURBT plus immediate intravesical chemotherapy (Table 1).

• The model assumed that all patients received MMC, since it accounts for over 80% of immediate intravesical chemotherapy

	Value	Source
	70,500	Jemal 2010
	70%	Witjes 2008
	83%	Cookson 2011
ne	53%	Tolley 1996
	36%	Tolley 1996

received a single instillation of MMC; 41% of patients received

• Costs were estimated using prevailing Medicare reimbursement rates for TURBT (\$1,982), BCG induction therapy (\$201 / instillation), MMC induction therapy (\$252 / instillation) and perioperative instillation of MMC (\$166 / instillation)

	Value	Source
	\$1,982.52	HOPPS
	\$166.15	CMS
	\$201.21	CMS
n)	\$252.42	CMS

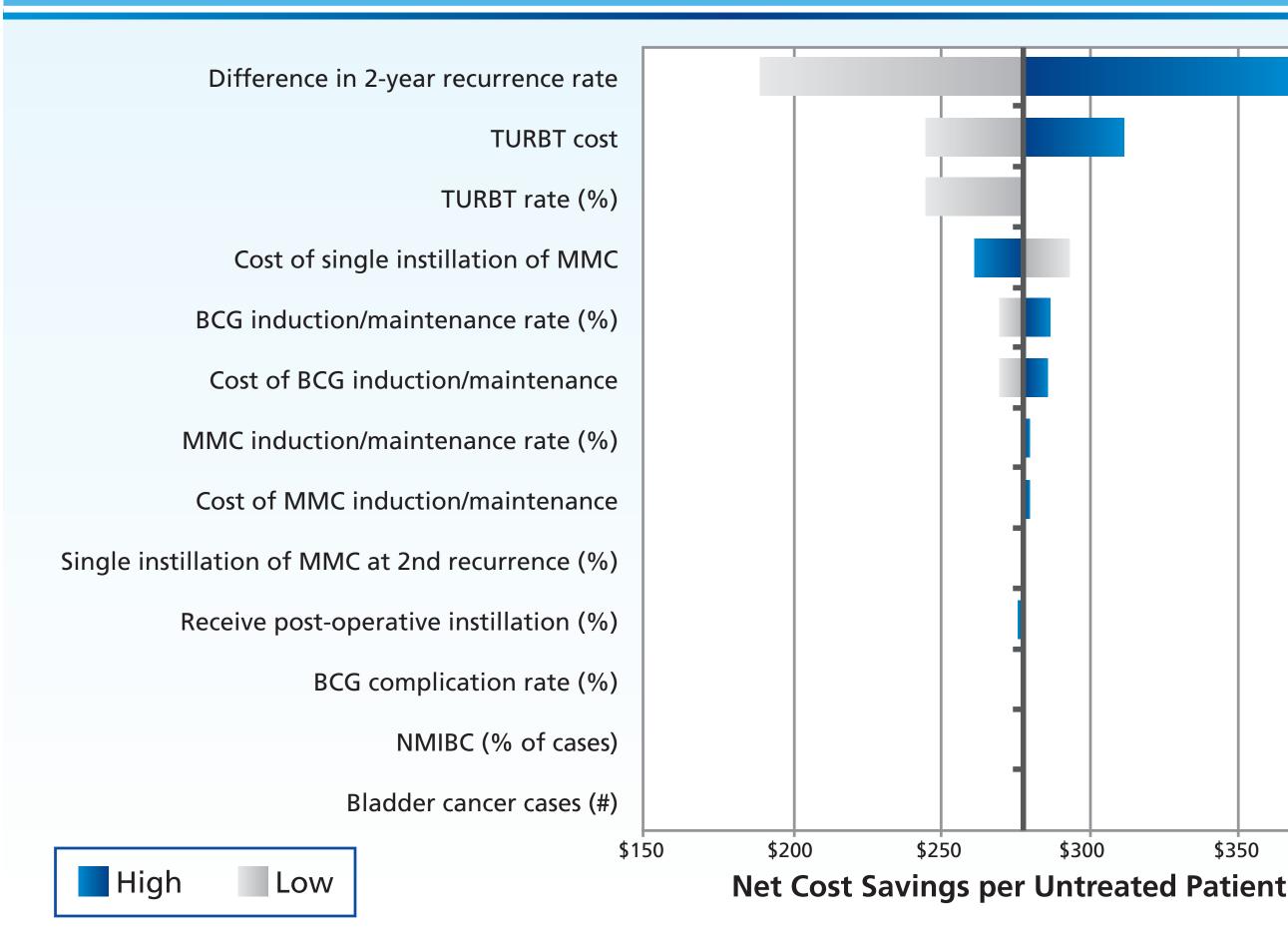
Sensitivity Analysis

- One-way sensitivity analyses were performed using the following key model inputs: population, utilization, and cost parameters.
- All base-case model parameters were varied by +/- 10% with the exception of the difference in 2-year recurrence rate, for which low (12.5%) and high values (28%) were available from the literature (Sylvester 2004, AUA 2007). (10% was selected a *priori* as the threshold for variation in model parameters without sufficient published data to allow enough change to yield meaningful results.)
- Results were plotted in a tornado diagram to illustrate the impact of the range of tested values on quality-adjusted days per untreated patient.

RESULTS

- The model estimates that approximately 41,000 patients diagnosed with NMIBC in 2010 did not receive an immediate post-operative instillation of chemotherapy.
- If treatment guidelines were followed, it is estimated that 6,963 NMIBC recurrences would be prevented annually.
- Each of these recurrences costs an estimated additional \$2,608, resulting in preventable medical costs exceeding \$18 million annually
- On a per patient basis, these results could lead to a cost savings of \$443 and a net savings of \$277, even after accounting for the added cost of an immediate MMC instillation.
- Results were most sensitive to the following parameters: difference in 2-year recurrence rate, TURBT cost, TURBT rate, and cost of a single MMC instillation.
- Despite these changes, model results were robust in that they yielded a net cost savings per untreated patient over the entire range of all tested value for all model parameters.
- Future research on the costs of alternative treatments for NMIBC should better assess recurrence rates and costs of both TURBT and instillation therapy.

Figure 2: One-Way Sensitivity Analysis: Economic Analysis



LIMITATIONS

- Recurrence rates for NMIBC are heterogeneous, and individual patient prognosis depends upon numerous clinical factors. Despite this heterogeneity, the difference in recurrence rates represents a population average, from a study which stratified the analysis across low-, medium-, and high-risk groups and found a similar relative benefit of MMC instillation in all risk groups (Tolley 1996).
- As with all modeling studies, combining data from different sources involves numerous assumptions. While the current study suggests that immediate post-operative instillation of chemotherapy would be cost-saving, additional research, such as a comparative effectiveness (aka pragmatic) trial would be necessary to demonstrate a real-world economic advantage.
- The model assumes that all newly diagnosed NMIBC patients are candidates for intravesical instillation. However, some patients may have high-grade tumors and may therefore be candidates for more aggressive therapy, such as BCG or even cystectomy. However, it was believed that this represents a small portion of newly diagnosed cases.
- The analysis does not include adverse events associated with a single immediate instillation. However, local effects, while common, are usually self-limiting and relatively minor, while systemic effects that may be severe tend to be infrequent (Koga 2006). Therefore, the costs of managing these adverse effects are likely to have minimal impact.

CONCLUSIONS

- Improved compliance with treatment guidelines from increased use of perioperative intravesical chemotherapy can reduce the economic burden of NMIBC.
- Use of a single immediate intravesical instillation of chemotherapy would be cost saving over a two-year time horizon.

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