Macro and Microeconomics of Blue Light Cystoscopy with CYSVIEW® in Non-Muscle Invasive Bladder Cancer (NMIBC)

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OBJECTIVE

To determine the estimated budget impact to practices that incorporate blue light cystoscopy (BLC) with hexaminolevulinate HCL (HAL) for the surveillance of non-muscle-invasive bladder cancer (NMIBC) in the clinic setting.

BACKGROUND

The American Cancer Society estimates more than 80,000 new cases of bladder cancer in 2020, making it the 6th most common cancer in the United States [1]. Majority of new cases are superficial or non-muscle-invasive bladder cancers (NMIBC) and are associated with five-year survival rates exceeding 70% [1].

The American Urological Association recommends ongoing surveillance for those diagnosed with NMIBC, including an initial surveillance cystoscopy within 3-4 months of treatment completion [2]. Critically, 50-70% of patients diagnosed with NMIBC will experience a recurrence of their tumor, with 10-20% advancing to become muscle-invasive disease [3].

In 2018, the FDA expanded the approved use of hexaminolevulinate HCl (HAL), marketed in the US as Cysview by Photocure Inc., in conjunction with blue-light cystoscopy (BLC) to include its use in the surveillance of non-muscle-invasive bladder cancer (NMIBC).

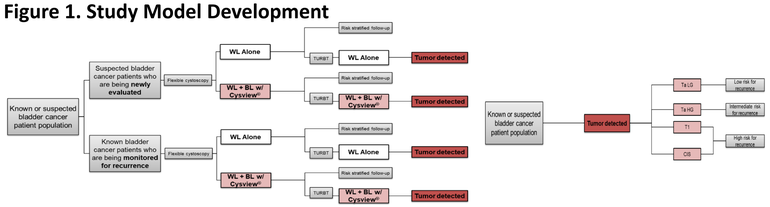
Evidence suggests that white light cystoscopy (WLC) can fail to detect cases of NMIBC as compared to blue light cystoscopy (BLC) [4, 5], with those undetected case progressing to a more serious form of cancer and aggressive interventions. Less effective surveillance using WLC may result in missed diagnoses and thus progressive disease, leading to higher costs associated with care and great impact on patients. This growing evidence suggests that BLC can impact risk stratification and disease management, but may also allow for higher quality, more-complete resections impacting disease outcomes in patients [6].

The potential cost-effectiveness of BLC in the management of NMIBC has been documented in the context of various healthcare settings globally, including France, Sweden and Canada [7-10]. In a US-based decision tree modelling study, BLC with HAL once again provided a more cost-effective approach to the management of patients with NMIBC; however this study was confined to the use of BLC in the hospital outpatient department setting [11].

METHODS

A budget impact model was developed from an academic medical system hospital outpatient department perspective to assess the projected costs and reimbursement at 2 years for a simulated facility with 50 newly diagnosed bladder cancer patients based on (Figure 1). The population of interest is quantified using published data on bladder cancer epidemiology, including the incidence of newly diagnosed bladder cancer cases, the percent of those tumors that are NMIBC, and the stage and grade of tumor [15-18].

Figure 1. Study Model Development



Cystoscopy performance inputs and downstream treatment response assumptions were based on existing published literature [3, 16].

All patients experienced a flexible cystoscopy follow-up visit as per the follow-up schedule that was pre-defined per risk group. The combination of technologies for the intervention or comparator affected the diagnostic test performance and thereby the risk of recurrence. Patients that experienced a detected recurrence would be referred to the OR for a transurethral resection of the bladder (TURBT). Patients that remained recurrence-free would have no further care at that time period and be reassessed at the next surveillance follow-up. After a TURBT and subsequent immediate treatment, patients restarted the follow-up schedule according to their perceived risk for recurrence (low, intermediate, and high).

Reimbursement was based on national average Medicare rates adjusted to the specific reimbursed rates of the base case clinic where applicable. Costs were inflated to 2020 dollars using previously established methods summing Medicare reimbursements, coinsurance reimbursements, perioperative chemotherapy, and patient-liability costs. Costs were assessed on geometric mean costs per ambulatory payment classification (APC) for a hospital-based outpatient department (HOPD), with assumed percent of reimbursement for the clinic [17-20] and are summarized in Table 1.

Table 1. Base Case Scenario Inputs: Costs in USD

COSTS	Office	Hospital Outpatient Department (Blue Light Cystoscopy with HAL)	Hospital Outpatient Department (White Light Cystoscopy)
52000/5372	$ 385.24	$ 572.21	$ 572.21
52204/5373	$ 350.62	$ 2,531.33	$ 2,088.13
52214/5373	$ 648.70	$ 2,531.33	$ 2,088.13
52224/5373	$ 677.90	$ 2,531.33	$ 2,088.13
52234/5374	[redacted]	$ 2,531.33	$ 2,531.33
52235/5374	[redacted]	$ 2,457.74	$ 2,457.74
52240/5375	[redacted]	$ 3,109.75	$ 3,109.75

Table 2 Base Case Scenario Inputs: Reimbursement

REIMBURSEMENT	Office	Hospital Outpatient Department (Blue Light Cystoscopy with HAL)	Hospital Outpatient Department (White Light Cystoscopy)
52000/5372	$ 280.00	$ 562.25	$ 562.25
52204/5373	$ 389.58	$ 2,894.00	$ 1,791.00
52214/5373	$ 720.78	$ 2,894.00	$ 1,791.00
52224/5373	$ 753.22	$ 2,894.00	$ 1,791.00
52234/5374	[redacted]	$ 2,894.00	$ 2,894.00
52235/5374	[redacted]	$ 2,960.50	$ 2,960.50
52240/5375	[redacted]	$ 5,435.00	$ 5,435.00

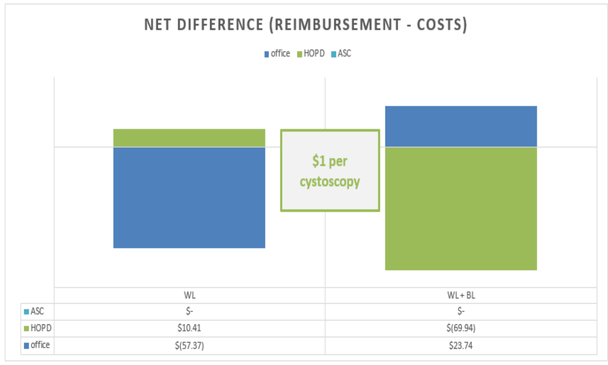
RESULTS

There were 38 TURBTS for initial detection, including 28 TA, 14 low risk (4 low grade intermediate risk, 10 high-grade intermediate risk), 5 T1 high risk and 4 CIS high risk.

Base case scenario outlined the comparison between current utilization of only WL cystoscopy versus future utilization of WL + BL cystoscopy in two practice settings (HOPD and Office), expressed as the net difference of reimbursement and costs. Institutions that utilized WL cystoscopy alone would see a $10.41 gain in the HOPD per cystoscopy, but a loss of $57.37 in the office per cystoscopy, leading to a loss of $46.94 per cystoscopy overall. Institutions that adopted WL + BL cystoscopy would see a $69.94 loss in the HOPD per cystoscopy, but a gain of $23.74 in the office per cystoscopy, leading to a loss of $46.20 per cystoscopy overall. Institutions that adopted WL + BL cystoscopy in both practice settings would see a ~ $1 increase in reimbursement than institutions that have WL cystoscopy alone (Figure 2).

Further, the use of BLC identified 9 additional recurrences over two years compared to WLC alone. Of those recurrences missed in the first year using WLC alone, approximately 1% would progress to a higher tumor grade.

Figure 2. Net Difference (Reimbursement – Costs) for White Light and White Light + Blue Light Cystoscopy Across Settings



ASC: Ambulatory Surgical Center, BL: Blue Light; HOPD: Hospital-Based Outpatient Department; WL: White Light

CONCLUSIONS

The current study suggests that the use of flexible BLC for the surveillance of NMIBC doesn't impact cost per cystoscopy. Additionally, flexible BLC resulted in the identification of 9 recurrences over two years that would otherwise be missed using WLC alone, resulting in more effective TURBTs and potentially lower progression disease rates. These findings could have important implications in the management of NIMBC and help guide clinical practice guidelines that promote cost-effective care and improved patient outcomes.

LIMITATIONS

The model employed assumed that follow-up cystoscopies and treatment were completed as per AUA guidelines; however, it's possible that individual urologists or patients may engage in varying follow-up periods and treatment. Also, individual practice volumes vary (i.e. community vs. academic) and our conservative case volume of 50 patients over 2 years may not accurately depict 'real world' practice volumes at certain centers. This study utilized National Medicare reimbursement rates in situations that focus practice data wasn't available; this may have underestimated reimbursement for those patients covered under private insurance. Medicare reimbursement rates can also change from year to year based on reevaluation of practice costs and the inclusion of new technology. With a lack of published data, it was assumed that the risk of recurrence in the 1st year and 2nd year would be identical, which may not be the case. Finally, it was assumed that the complete conversion of patients from being assessed with WLC to 100% evaluated with BLC, whereas in real-world clinical practice, there may be mixed use depending on patient or urologist preference.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2020. Atlanta, Ga: American Cancer Society; 2020.
2. Chang SS, Boorjian SA, Chou R, Clark PE, Daneshmand S, Konety BR, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. The Journal of urology. 2016;196:1021-9.
3. Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffioux C, Denis L, et al. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. European urology. 2006;49:466-5; discussion 75-7.
4. Vartolomei L, Ferro M, Mirone V, Shariat SF, Vartolomei MD. Systematic Review: Depression and Anxiety Prevalence in Bladder Cancer Patients. Bladder Cancer. 2018;4:319-26.
5. Rink M, Babjuk M, Catto JW, Jichlinski P, Shariat SF, Stenzl A, et al. Hexyl aminolevulinate-guided fluorescence cystoscopy in the diagnosis and follow-up of patients with non-muscle-invasive bladder cancer: a critical review of the current literature. European urology. 2013;64:624-38.
6. Witjes JA, Babjuk M, Gontero P, Jacqmin D, Karl A, Kruck S, et al. Clinical and cost effectiveness of hexaminolevulinate-guided blue-light cystoscopy: evidence review and updated expert recommendations. European urology. 2014;66:863-71.
7. Klaassen Z, Li K, Kassouf W, Black PC, Dragomir A, Kulkarni GS. Contemporary cost-consequence analysis of blue light cystoscopy with hexaminolevulinate in non-muscle-invasive bladder cancer. Can Urol Assoc J. 2017;11:173-81.
8. Lotan Y, Chaplin I, Ahmadi H, Meng X, Roberts S, Ladi-Seyedian S, et al. Prospective evaluation of blue-light flexible cystoscopy with hexaminolevulinate in non-muscle-invasive bladder cancer. BJU international. 2020.
9. Rose JB, Armstrong S, Hermann GG, Kjellberg J, Malmström PU. Budget impact of incorporating one instillation of hexaminolevulinate hydrochloride blue-light cytoscopy in transurethral bladder tumour resection for patients with non-muscle-invasive bladder cancer in Sweden. BJU international. 2016;117:E102-13.
10. Roupêret M, Malavaud B, Molinier L, Leleu H, Blachier M, Marteau F. [Cost-effectiveness of transurethral resection of the bladder with blue light in patients with non muscle invasive bladder cancer in France]. Prog Urol. 2015;25:256-64.
11. Garfield SS, Gavaghan MB, Armstrong SO, Jones JS. The cost-effectiveness of blue light cystoscopy in bladder cancer detection: United States projections based on clinical data showing 4.5 years of follow up after a single hexaminolevulinate hydrochloride instillation. The Canadian journal of urology. 2013;20:6682-9.
12. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65.
13. Aldousari S, Kassouf W. Update on the management of non-muscle-invasive bladder cancer. Can Urol Assoc J. 2010;4:56-64.
14. Heney NM, Ahmed S, Flanagan MJ, Frable W, Corder MP, Hafermann MD, et al. Superficial bladder cancer: progression and recurrence. The Journal of urology. 1983;130:1083-6.
15. Jakse G, Loidl W, Seeber G, Hofstädter F. Stage T1, grade 3 transitional cell carcinoma of the bladder: an unfavorable tumor? The Journal of urology. 1987;137:39-43.
16. Cambier S, Sylvester RJ, Collette L, Gontero P, Brausi MA, van Andel G, et al. EORTC Nomograms and Risk Groups for Predicting Recurrence, Progression, and Disease-specific and Overall Survival in Non-Muscle-invasive Stage Ta-T1 Urothelial Bladder Cancer Patients Treated with 1-3 Years of Maintenance Bacillus Calmette-Guérin. European urology. 2016;69:60-9.
17. Centers for Medicare & Medicaid Services. Hospital Outpatient PPS. 2020.
18. Centers for Medicare & Medicaid Services. Physician Fee Schedule. 2020.
19. Centers for Medicare & Medicaid Services. Ambulatory Surgical Center (ASC) Payment. 2020