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Patient-reported outcomes of blue-light flexible cystoscopy with hexaminolevulinate in the surveillance of bladder cancer: results from a prospective multicentre study

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Objective

To evaluate blue-light flexible cystoscopy (BLFC) with hexaminolevulinate in the office surveillance of patients with non-muscle-invasive bladder cancer with a high risk of recurrence by assessing its impact on pain, anxiety, subjective value of the test and patient willingness to pay.

Materials and Methods

A prospective, multicentre, phase III study was conducted during which the Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety, Pain and 'Was It Worth It' questionnaires were administered at baseline, after surveillance with BLFC and after resection for those referred to the operating room. Comparisons of scores were performed between groups.

Results

A total of 304 patients were enrolled, of whom 103 were referred for surgical examination. Of these, 63 were found to have histologically confirmed malignancy. Pain levels were low throughout the study. Anxiety levels decreased after BLFC ($\Delta = -2.6$), with a greater decrease among those with negative pathology results ($P = 0.051$). No differences in anxiety were noted based on gender, BLFC results, or test performance (true-positive/false-positive). Most patients found BLFC 'worthwhile' (94%), would 'do it again' (94%) and 'would recommend it to others' (91%), with no differences based on BLFC results or test performance. Most patients undergoing BLFC (76%) were willing to pay out of pocket.

Conclusions

Anxiety decreased after BLFC in patients with negative pathology, including patients with false-positive results. Most of the patients undergoing BLFC were willing to pay out of pocket, found the procedure worthwhile and would recommend it to others, irrespective of whether they had a positive BLFC result or whether this was false-positive after surgery.

Keywords

fluorescence cystoscopy, recurrence, CIS, PRO, patient-reported outcomes, #blcsm, #BladderCancer

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Introduction

As bladder cancer is associated with a high rate of recurrence after transurethral resection of bladder tumour (TURBT), patients undergo regular follow-up cystoscopies, usually every 3–6 months [1]. Surveillance is usually performed as an office-based procedure with white-light flexible cystoscopy (WLFC). A recent meta-analysis evaluated blue-light cystoscopy (BLC) in 14 randomized controlled trials, including nine with hexaminolevulinate (HAL; Photocure ASA, Oslo, Norway) [2], confirming that BLC improved detection of papillary tumours and carcinoma *in situ* (CIS) compared with white-light cystoscopy (WLC). Compared with WLC, BLC detected at least one additional Ta/T1 tumour in 24.9% of patients, and at least one CIS lesion was only seen in blue light in 26.7% of patients ($P < 0.001$) [3]. Based on available data, the AUA guidelines for non-muscle-invasive bladder cancer (NMIBC) state that 'in a patient with NMIBC, a clinician should offer blue-light cystoscopy at the time of TURBT, if available, to increase detection and decrease recurrence (Moderate Recommendation; Grade B)' [1].

Because WLC can miss tumours during surgery, it may also miss tumours in the office setting. In Europe, a flexible photodynamic diagnosis videoscope (KARL STORZ D-Light C Photodynamic Diagnosis Flexible Videoscope System) has been used with HAL (marketed as Hexvix in Europe and Cysview in the USA and Canada). A recent phase III clinical study in the USA demonstrated improved detection of bladder cancer with this technique during office surveillance [4].

Cost implications and the trade-off between improved sensitivity and false-positive results are often analysed years after incorporating the technology. Our objective was to measure prospectively the impact of blue-light flexible cystoscopy (BLFC) with HAL on patient satisfaction, anxiety, and willingness to pay by conducting a prospective phase III, comparative, multicentre study.

Materials and Methods

Study Design

This was a prospective, open-label, comparative within-patient controlled phase III study conducted in 17 centres in the USA. The study was performed in accordance with Good Clinical Practice and the Declaration of Helsinki. Written approval was obtained from the relevant institutional review board at each study site, and all patients gave fully informed written consent before enrolment in the study.

Patients

Patients with a history of multiple, recurrent or high grade bladder tumours were eligible if they had a history of histologically confirmed tumour, either from a TURBT or a previous surveillance cystoscopy. Patients were excluded if they had received BCG immunotherapy or intravesical chemotherapy in the preceding 6 weeks.

Examination Process

After screening and enrolment, patients returned for the first office-based surveillance visit where they received an instillation of HAL and underwent flexible cystoscopy, first with white light, then with blue light, using local anaesthesia [4]. A few patients ($n = 8$) were randomized to receive WLFC only (to ensure a thorough inspection would be carried out with white light alone), and data from the screening and post-surveillance questionnaires were included in the analysis. The remaining patients underwent BLFC. Patients with suspicious findings using either examination method were referred to the operating room for a cystoscopy with biopsy which was carried out within 6 weeks of the surveillance visit.

In the operating room, all patients received another HAL instillation and the bladder was inspected with rigid cystoscopy with white then blue light under general anaesthesia. All suspicious lesions were mapped at both inspections. Biopsies were taken of all suspicious lesions, and resection was carried out according to normal clinical practice.

All biopsies were analysed by a local pathologist and verified by a pathology consensus panel using the 2004 WHO/International Society of Urological Pathology consensus classification [4] and the 2002 TNM classification for staging of bladder cancer [5]. The consensus panel result was used for assessment of the efficacy endpoints, but the local pathology results were the findings communicated to patients.

Survey Procedure

Given that patients undergoing BLFC would receive an additional catheterization with instillation of Cysview, resulting in a longer waiting time for their procedure, we hypothesized that pain and anxiety may be negatively impacted. Patients were therefore asked about their levels of anxiety and pain at three time points: (1) at the screening visit; (2) immediately after surveillance cystoscopy; and (3), for those referred to the operating room, after they had received the pathology findings and were aware of their diagnosis. Subjective value of the test and willingness to pay were evaluated at the second and third time points. All surveys were administered via interview by the trained research coordinator.

Anxiety related to the diagnosis was measured using the Patient-Reported Outcomes Measurement Information System (PROMIS) [6] Anxiety 4a short-form questionnaire in which patients responded to the four statements in Table S1 [7,8].

Pain was measured using the PROMIS Pain Intensity 1a on a scale from 0 (no pain) to 10 (worst imaginable pain) in response to the questions in Table S2 (which differed based on the time point in the study). Total scores range from 0 to 100, with higher scores indicating worse anxiety and pain. PROMIS instruments are publicly available on the PROMIS Assessment Centre Library website (Table S3).

After surveillance and after referred patients had received their pathology results, patients were asked to respond to the questions in Table S4 relating to their experience of the procedure and willingness to pay using the 'Was It Worth It?' questionnaire [9].

Assessments and Statistical Analysis

The population for analysis included all patients who underwent surveillance cystoscopy. Some patients had been enrolled for training purposes (n = 68), while others were randomized out of the study (n = 8) as they only underwent WLFC, as described above in the methods section [4]. All were eligible for the post-surveillance survey; however, only those who were randomized to BLFC and required an operating room visit were eligible for the postoperative procedure survey.

Results

Patients

The study included 304 patients, including 68 patients who were enrolled as the training set (Table 1). Two-thirds of the patients had high grade cancer detected at their last TURBT, and the mean number of prior recurrences before entry to the study was 1.7. Two-thirds of patients had prior BCG or chemotherapy between 6 weeks and 90 days before surveillance cystoscopy. At baseline, 262/304 patients who underwent flexible cystoscopy (86%) completed the baseline survey, and 260 (85%) completed the post-surveillance survey. Among 103 patients referred to the operating room for suspicion of recurrence, 92 (89%) completed the postoperative procedure survey. A consort diagram showing patient flow has been previously published [4].

Tumour Detection

After surveillance cystoscopy, 103 patients were referred for cystoscopy and biopsy with suspicion of malignancy, and 63 were confirmed to have recurrence. BLFC was found to improve overall cancer detection by 20.6% [4]. Forty out of 220 patients had false-positive findings in the surveillance setting; 20 had false-positive findings with WLFC (9.1%) and the remaining 20 had false-positive findings with BLFC (9.1%).

Survey Results

Anxiety

The mean (SD) baseline PROMIS anxiety score was 51.8 (9.2), which decreased after surveillance by 2.6 points. A greater decrease was noted among patients with a negative BLFC result vs positive, with a trend towards significance (P = 0.051; Table 2). For patients referred to the operating room, overall anxiety decreased by 1.6 points compared with the score after surveillance, driven mainly by lower anxiety scores among patients with negative biopsies (P = 0.054).

No differences in anxiety scores were noted between men and women when evaluating change from baseline to post-surveillance (P = 0.63) or postoperatively (P = 0.56). In patients with intermediate-risk disease, positive BLFC was associated with an increase in anxiety, while negative BLFC was associated with a decrease. Patients with high-risk disease had a decrease in anxiety regardless of BLFC findings.

Pain

There was no time point pre- or post-surgery when the pain was impacted by intervention or BLFC. The mean (SD) pain scores were low for patients at baseline (0.6 [1.51]), post-surveillance (1.1 [1.92] and postoperatively (1.4 [2.13]). No change in post-surveillance pain from baseline was noted among those with positive or negative BLFC (P = 0.11). No differences in pain scores were noted between men and women when evaluating change from baseline to post-surveillance (P = 0.16) or postoperatively (P = 0.67), regardless of BLFC result (positive/negative) or performance (true-positive/false-positive; P = 0.45).

Perceived Value

Most of the patients found the BLFC experience worthwhile and would repeat the procedure and/or recommend it to others (Table 3). Patients' perception changed very little

Table 1 Demographics and baseline characteristics of the surveillance cystoscopy population (N = 304).

Age, years	Mean (SD)	69.0 (10.40)
	Median (min, max)	70.0 (35.92)
Men, n (%)		242 (79.6)
Women, n (%)		62 (20.4)
Race, n (%)	White	272 (89.5)
	Black	20 (6.6)
	Asian	10 (3.3)
	Other	0
Ethnicity, n (%)	Hispanic or Latino	6 (2.0)
	Non-Hispanic or Latino	296 (97.4)
Height, cm	Mean (SD)	174.1 (9.23)
	Median (min, max)	175.0 (145, 198)
Weight, kg	Mean (SD)	89.7 (19.48)
	Median (min, max)	87.8 (45, 160)

Table 2 PROMIS Anxiety scores for patients at baseline, post-surveillance and postoperatively.

	Statistic	Baseline	Post-surveillance	Postoperatively	Post-surveillance change from baseline	Postoperative change from post-surveillance
Anxiety (composite)	*N*	262	260	92	252	89
	Mean	51.8	49	48.7	−2.6	−1.6
Positive BLFC*	*N*	91	97	–	91	–
	Mean	51.6	50.4	–	−1.2	–
Negative BLFC*	*N*	115	111	–	110	–
	Mean	51.8	48.1	–	−3.5*	–
True-positive BLFC†	*N*	–	49	49	–	–
	Mean	–	51.0	50.6	–	0.1
False-positive BLFC†	*N*	–	44	43	–	–
	Mean	–	49.7	46.6	–	−3.4†

*BLFC, blue-light flexible cystoscopy.*Comparison between patients with positive BLFC and negative BLFC, P = 0.051. †Comparison between patients with and without confirmed malignancy, P = 0.054.*

based on the BLFC result (positive/negative) or performance (true-positive/false-positive).

Quality of Life/Expectations

Most patients undergoing BLFC (99%) reported either improved or stable quality of life (QoL) overall when compared with their baseline before the BLFC (Table 4). Improved QoL was reported more frequently among those with a negative BLFC (54%) compared with a positive BLFC (28%; $P < 0.001$). Similarly, improved QoL was reported more frequently among those with a false-positive (49%) compared with a true-positive result (18%; $P = 0.003$).

With regard to expectations, 60% of patients undergoing BLFC reported that their experience was better than expected (Table 4). This was more frequently reported by those with a negative BLFC (68%) vs positive (50%; $P = 0.01$); however, no significant differences were noted based on test performance.

Willingness to Pay

Most patients were willing to pay out of pocket for BLFC (Fig. 1). Among those willing to pay, 148/246 patients (60%) post-surveillance and 51/91 patients (56%) postoperatively were willing to pay $100 or more (Fig. 1). Only 59/246 patients (24%) post-surveillance and 26/91 patients (29%) postoperatively were unwilling to pay out of pocket for BLFC. When stratifying patients by age, sex and risk group, similar patterns emerged for the post-surveillance and postoperative populations. Most patients were willing either to pay $0 or to pay $100 out of pocket costs with a smaller proportion of patients reporting other cost thresholds (e.g. $25, $50, $200 or >$200).

Discussion

A prospective multicentre study found that BLFC improved the detection of bladder cancer in the outpatient setting, with a 20.6% increase in detection among those undergoing BLFC [4]. From a patient perspective, improved detection is weighed against an additional catheterization and the potential for a false-positive finding. As such, it is important to include patient-reported outcomes (PROs) in the assessment of the value of BLFC. Understanding value is a key reason that PRO measurement is increasingly common among oncology clinical trials [10,11]. In the present study, we report PROs of patients undergoing BLFC, highlighting anxiety, pain, perceived value and willingness to pay in the context of test accuracy and patient characteristics. We found that anxiety decreased after the BLFC procedure with no statistically significant differences based on gender. Pain scores were low among those undergoing the BLFC procedure. QoL and expectations were stable or improved among most patients undergoing BLFC (compared with pre-BLFC), influenced by the possibility (or reality) of cancer recurrence, and most patients considered the procedure worthwhile and were willing to pay money out of pocket.

Patients undergoing BLFC reported decreased anxiety (−2.6 points) and this was more pronounced among those with negative vs positive findings. In a study among diverse clinical samples including cancer, a PROMIS anxiety score change between 1.9 and 2.7 was deemed clinically significant, suggesting that the decrease in anxiety among patients who underwent BLFC is meaningful [12]. A minimal clinically important difference of 2.5 has been noted among other patient populations as well, including patients with chronic pain [13]. Because cancer can be missed by white light alone, it is probably more reassuring when the WLFC and BLFC are both negative. Alternatively, a negative cancer result (regardless of technology) may also be responsible for decreased anxiety. Likewise, those with positive findings had anxiety that may have been related to detection of cancer recurrence. Our data support the influence of biopsy results on anxiety. Although those with true-positives had stable anxiety rates (−0.4) from time of surveillance to post-biopsy, those with false-positives had a further, clinically meaningful decrease in anxiety (−3.4),

Table 3 Perceived procedure value stratified by blue-light flexible cystoscopy result and performance.

	Overall post-surveillance *n* (%)	Overall postoperatively *n* (%)	Post-surveillance sample			Postoperative sample		
			Positive BLFC *n* (%)	Negative BLFC *n* (%)	*P*	True-positive *n* (%)	False-positive *n* (%)	*P*
Was it worthwhile?	195 (94)	80 (87)	88 (91)	107 (97)	0.07	43 (88)	37 (86)	1.0
Would you do it again?	195 (94)	84 (91)	89 (92)	106 (96)	0.23	45 (92)	39 (91)	1.0
Would you recommend to others?	188 (91)	83 (90)	87 (90)	101 (92)	0.64	43 (88)	40 (93)	0.49

BLFC, blue-light flexible cystoscopy.

Table 4 Quality of life and expectations stratified by blue-light flexible cystoscopy result and performance.

	Overall post-surveillance, *n* = 202	Overall postoperatively, *n* = 92	Post-surveillance sample			Postoperative sample		
			Positive BLFC, *n* = 92	Negative BLFC, *n* = 110	*P*	True-positive, *n* = 49	False-positive, *n* = 43	*P*
Did your QoL change by undergoing BLFC?								
Improved	85 (42)	30 (33)	26 (28)	59 (54)	0.0003	9 (18)	21 (49)	0.003
Same	116 (57)	58 (63)	65 (71)	51 (46)		38 (78)	20 (47)	
Worse	1 (1)	4 (4)	1 (1)	0 (0)		2 (4)	2 (5)	
	N = 206	*N* = 91	*N* = 96	*N* = 110	*P*	*N* = 48	*N* = 43	*P*
How was your experience after BLFC compared with what you expected?								
Better	123 (60)	37 (41)	48 (50)	75 (68)	0.0103	17 (35)	20 (47)	0.295
Same	79 (38)	51 (56)	45 (47)	34 (31)		30 (63)	21 (49)	
Worse	4 (2)	3 (3)	3 (3)	1 (1)		1 (2)	2 (5)	

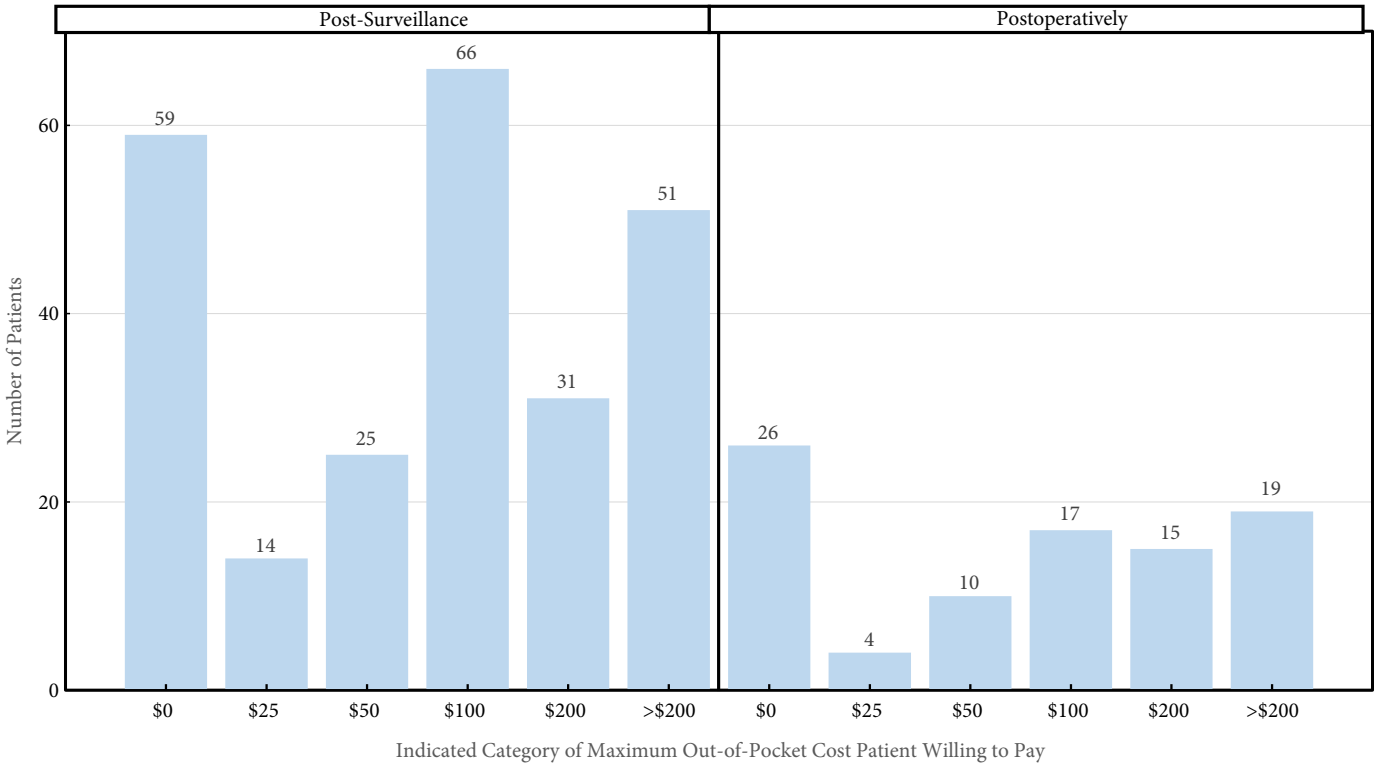
BLFC, blue-light flexible cystoscopy. Values are n (% responding yes). Abbreviations: BLFC, blue-light flexible cystoscopy; HAL, hexaminolevulinate; TURBT, transurethral resection of bladder tumour; WLFC, white-light flexible cystoscopy; BLC, blue-light cystoscopy; CIS, carcinoma in situ; NMIBC, non-muscle-invasive bladder cancer; PROMIS, Patient-Reported Outcomes Measurement Information System; QoL, quality of life; PRO, patient-reported outcome.

suggesting that either BLFC provides additional reassurance regarding their results or that a 'true'-negative biopsy decreases anxiety (or both). Although differences between true- and false-positives did not reach statistical significance, a clinically meaningful difference of 3 points (beyond the minimally important difference of 2.5) between groups suggests that a new cancer recurrence affects anxiety, as would be expected. Without a WLC comparator, understanding the additive impact of BLFC on anxiety, beyond the impact of cancer is difficult to ascertain. Our results do suggest, however, that BLFC (with an added procedure and instillation) does not negatively impact anxiety or pain, which is reassuring. Furthermore, although patients undergoing BLFC had an additional procedure (catheterization) and instillation (HAL), all pain scores remained low throughout the study (post-surveillance and postoperatively) which is encouraging given its improvement in cancer detection.

Additional measures of interest included QoL and expectations regarding the procedure. QoL either remained stable or improved among most patients with BLFC, with greater improvement in those with negative BLFC findings. Interestingly, improved QoL was more pronounced among those with false-positive (rather than true-positive) findings. QoL differences may be more reflective of a possible cancer recurrence rather than of the test itself. Uncertainty regarding a cancer diagnosis can influence perception, such as QoL and expectations [14]. Among patients with RCC undergoing watchful waiting, illness uncertainty (as measured by the Mishel Uncertainty in Illness Scale) was negatively associated with general QoL, cancer-specific QoL and distress [15]. Our results support the idea that reducing uncertainty regarding diagnosis increases QoL. Communicating around uncertainty should be considered in patient counselling during NMIBC surveillance and testing. Again, understanding the additive impact of BLFC to cancer recurrence is difficult without a randomized comparator, but our results suggest that BLFC does not negatively impact QoL despite additional catheterization and instillation.

Although QoL and expectations differed according to test result and performance, perceived value did not differ in the same way. Most of the patients found the BLFC experience worthwhile and would repeat the procedure and/or recommend to others. The overall positive perception of value was reflected in the proportion of patients who were willing

Fig. 1 Patient maximum willingness to pay for blue-light flexible cystoscopy.



to pay money out of pocket, regardless of patient characteristics. This has important policy implications regarding patient charges and reimbursement. While the range of costs that were used would not be sufficient to pay for the entire procedure 'out of pocket', costs are still relatively high when compared with most co-pays for insurance companies and Medicare.

The present study has several limitations. First, we attempted to minimize the number of questions to limit respondent burden while retaining accuracy of measurement. The short-form items, although responsive, may not detect nuances regarding pain and anxiety. The PROMIS questionnaires have been validated such that they may be used in any patient population; however, studies on the use of the PROMIS questionnaire in a cystoscopy or bladder cancer surveillance population have not been published. Furthermore, although the Was It Worth It questionnaire has been used in colorectal and breast cancer clinical trials, validation has not yet been performed. Nevertheless, it is the only existing questionnaire that measures patient-perceived 'worth' of an intervention. A larger, validated QoL questionnaire was intentionally excluded to limit questions and survey burden. Arguably, qualitative interviews would provide richer data regarding patient perception and could represent an avenue for future research. Finally, this study did not include a WLFC comparator with which to compare anxiety, pain and QoL. Nevertheless, we were able to compare these changes with baseline (pre-procedure), and our findings show that BLFC did not negatively (and may positively) impact PROs. Despite these limitations, the present study is the first to report PROs regarding BLFC and to suggest that patients value the procedure and are willing to pay out of pocket, reporting minimal effects on pain and anxiety.

In conclusion, in the present phase III, prospective, multicentre, within-patient controlled study among patients with NMIBC, anxiety decreased after BLFC when compared to baseline, and was more pronounced among those with negative pathology, including those with false-positive results, supporting the impact of cancer recurrence on anxiety. Most patients undergoing BLFC were willing to pay out of pocket, found it worthwhile to undergo the procedure and would recommend it to others, irrespective of whether they had a positive BLFC or a false-positive result postoperatively. BLFC improves overall cancer detection by 20.6% and does not adversely impact PROs, supporting its routine use in surveillance for NMIBC at high risk of recurrence.

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References

1 **Chang SS, Boorjian SA, Chou R et al.** Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline. *J Urol* 2016; 196: 1021–9

2 **Chou R, Selph S, Buckley DI et al.** Comparative effectiveness of fluorescent versus white light cystoscopy for initial diagnosis or surveillance of bladder cancer on clinical outcomes: systematic review and meta-analysis. *J Urol* 2017; 197: 548–58

3 **Burger M, Grossman HB, Droller M et al.** Photodynamic diagnosis of non-muscle-invasive bladder cancer with hexaminolevulinate cystoscopy: a meta-analysis of detection and recurrence based on raw data. *Eur Urol* 2013; 64: 846–54

4 **Daneshmand S, Patel S, Lotan Y et al.** Efficacy and safety of blue light flexible cystoscopy with hexaminolevulinate in the surveillance of bladder cancer: a phase III, comparative, multicenter study. *J Urol* 2018; 199: 1158–65

5 **Edge SB, Compton CC, Fritz AG, Greene FL, Trotti A III** eds. *AJCC Cancer Staging Handbook*, 7th edn. New York, NY: Springer, 2010.

6 Patient-Reported Outcomes Measurement Information System. Anxiety: a brief guide to the PROMIS Anxiety instruments. In: Initiative NIoHNPR, ed. NIH, 2015. Available at: https://wwwassessmentcenternet/documents/PROMIS%20Anxiety%20Scoring%20Manualpdf. Accessed May 2018

7 **Driban JB, Morgan N, Price LL, Cook KF, Wang C.** Patient-Reported Outcomes Measurement Information System (PROMIS) instruments among individuals with symptomatic knee osteoarthritis: a cross-sectional study of floor/ceiling effects and construct validity. *BMC Musculoskelet Disord* 2015; 16: 253

8 **Cella D, Choi S, Garcia S et al.** Setting standards for severity of common symptoms in oncology using the PROMIS item banks and expert judgment. *Qual Life Res* 2014; 23: 2651–61

9 **Sloan JA, Mahoney M, Sargent JM et al.** Was it worth it (WIWI)? Patient satisfaction with clinical trial participation: Results from North Central Cancer Treatment Group (NCCTG) phase III trial N0147. ASCO Annual Meeting: *J Clin Oncol* 2011 (suppl; abstr 6122); 29: 6122

10 **Basch E, Abernethy AP, Mullins CD et al.** Recommendations for incorporating patient-reported outcomes into clinical comparative effectiveness research in adult oncology. *J Clin Oncol* 2012; 30: 4249–55

11 **Garcia SF, Cella D, Clauser SB et al.** Standardizing patient-reported outcomes assessment in cancer clinical trials: a patient-reported outcomes measurement information system initiative. *J Clin Oncol* 2007; 25: 5106–12

12 **Schalet BD, Pilkonis PA, Yu L et al.** Clinical validity of PROMIS depression, anxiety, and anger across diverse clinical samples. *J Clin Epidemiol* 2016; 73: 119–27

13 **Kroenke K, Yu Z, Wu J, Kean J, Monahan PO.** Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. *Pain Med* 2014; 15: 1892–901

14 **Gramling R, Stanek S, Han PKJ et al.** Distress due to prognostic uncertainty in palliative care: frequency, distribution, and outcomes among hospitalized patients with advanced cancer. *J Palliat Med* 2018; 21: 315–21

15 **Parker PA, Alba F, Fellman B et al.** Illness uncertainty and quality of life of patients with small renal tumors undergoing watchful waiting: a 2-year prospective study. *Eur Urol* 2013; 63: 1122–7

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Questions relating to anxiety.
Table S2. Questions relating to pain.
Table S3. Scoring scheme for PROMIS measures.
Table S4. Questions relating to the patient experience of blue light cystoscopy.

