

Elicitation of Health State Utilities Associated with Progression from BCG-unresponsive NMIBC

Prepared by:

Cooper O,¹ Rentz A,² Piglowska N,¹ Smith C,¹ Jakobsen J,³ Catto J,⁴ Niegisch G,⁵ Ghatnekar O,⁴ Swinburn P¹

¹Evidera, London, UK; ²Evidera, Bethesda, MD, USA; ³Ferring Pharmaceuticals A/S, Copenhagen, Denmark; ⁴University of Sheffield, Sheffield, UK; ⁵Heinrich-Heine-Universität, Düsseldorf, Germany



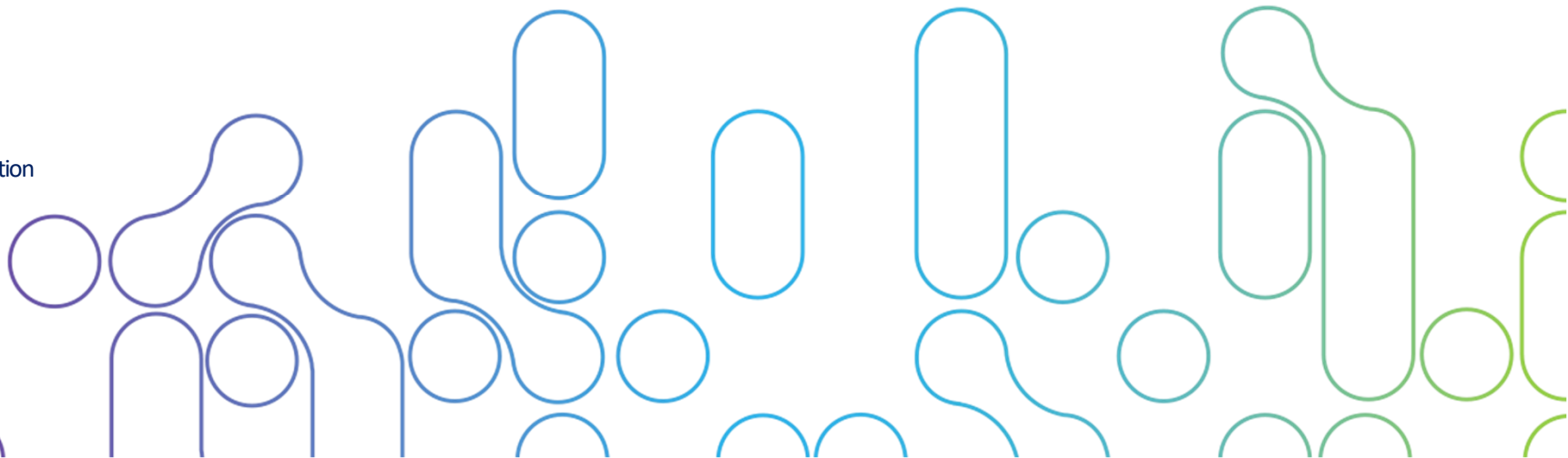
Prepared for:

ISPOR 2022 Podium Presentation



Monday, May 16, 2022

© 2022 Evidera. All Rights Reserved.



Introduction



Non-Muscle Invasive Bladder Cancer (NMIBC)



Health States



Objectives and Utility Scores



Results



Methods



Discussion and Conclusion

Non-Muscle Invasive Bladder Cancer (NMIBC)

- Bladder cancer is the most common cancer of the urinary tract, accounting for 3% of all cancer diagnoses and 3% of all cancer deaths in the United Kingdom (UK) ^{1,2}. Bladder cancer is more common in males than females, with four times as many diagnoses in males compared to females. ³
- Non-muscle-invasive bladder cancer (NMIBC) is a cancer located on the tissue that lines the inside of the bladder and does not involve the bladder muscle. About 2/3 of patients are diagnosed with NMIBC, and another third with muscle-invasive bladder cancer (MIBC) which has a poor prognosis (new-4). ⁴ There are few available treatments for high-risk NMIBC. ⁵
- Typical first-line treatments include:
 - Trans-urethral resection of bladder tumour (TURBT)
 - Chemotherapy
 - Bacillus Calmette-Guerin (BCG) intravesical therapy administered directly into the bladder. ⁶
- More advanced interventions for BCG unresponsive patients include:
 - Radical cystectomy: The entire urinary bladder and surrounding tissue are removed surgically, which is potentially curative. ⁶ Having a radical cystectomy has long-term irreversible impacts to patients, requiring them to use a stoma bag or neo-bladder for the rest of their lives. Complications include but are not limited to urinary tract infections and body image issues.
- At present, there is an urgent need for novel agents of treatment for NMIBC that can help slow progression of the illness while sparing the bladder. ⁷

Utility scores and Objectives

Objective:

- The purpose of this study was to elicit the general public's perspective on QoL, measured as utility scores, associated with treatment for BCG-unresponsive NMIBC and disease progression.
- Reimbursement decisions for new therapies in many markets are based on the relationship between the cost implications and quality of life (QoL) benefit that the new therapy confers.
- Perceived QoL implications of different health states can be assessed using a variety of methods time and can be conducted with members of the general public to produce societal "*utility*" values:
 - 1 represents full health.
 - 0 represents a state equivalent to death.
 - <1 represents a state that is worse than dead.
- **Utility scores** are values between 1 and -1 that represent the preferences of different disease health state descriptions.

Methods

- Phase I. Pilot Study → To develop and test bladder cancer health states:
 - Interviews were conducted with:
 - Three clinicians
 - A patient advisor
 - 30 members of the general public (as a pilot stage of the TTO exercise)
 - Interview findings were used to finalize the health states.
- Phase II. Main Study → To elicit utility scores:
 - Vignette-based TTO utility interviews were conducted in person with a sample of participants from the general public in London, United Kingdom (UK).
 - Participants were asked to rank four chronic health states describing different bladder cancer scenarios in order of preference, followed by the TTO valuation exercise for all five health states.
 - A demographic and clinical information form was completed by participants at the end of the utility interview.
 - The EQ-5D-5L questionnaire was also completed; this is a self-administered, generic, preference-weighted measure designed to assess health status⁸
- TTO is a choice-based method of eliciting health state utility, which reflects the length of remaining life an individual may be prepared to trade to avoid remaining in a health state that is less than full health. The states in this instance describe scenarios associated with bladder cancer.

Health States

- Health states differed in terms of the severity of bladder cancer symptoms' severity, treatment and impacts. Health states were either “chronic” (valued in the TTO task with a 10-year time horizon) or “path “(one-year time horizon). Path health states had a shorter time horizon due to the transitional nature of recovery from the cystectomy procedure.
- Chronic
 - T: No High-Grade Recurrence
 - L: High-Grade Recurrence
 - W: >1-year Post-cystectomy
 - H: MIBC with Metastatic Disease
- Path
 - D: First Year Post-cystectomy (male)
 - G: First Year Post-cystectomy (female)

*Each health state was assigned a random letter as an identifier (T, L, W, H, D or G)

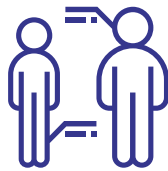
Health State Example : T – No high-grade Recurrence

T	
Description	<ul style="list-style-type: none"> The cancer cells have responded to the treatment and are either no longer present or not considered to be a risk.
Symptoms	<ul style="list-style-type: none"> You will likely not experience any symptoms at all. <ul style="list-style-type: none"> If you do experience symptoms, they may include blood in your urine and the need to pee more frequently with some urgency, which may be accompanied by a burning or stinging pain. They may also include reduced bladder capacity (a reduction in the amount of urine your bladder can store before you feel the need to empty it).
Treatment and Management	<ul style="list-style-type: none"> You will need to go to the hospital/outpatient clinic every 3 months to receive an experimental treatment, which will be inserted into your bladder for 1 hour. You will need to go to the hospital/outpatient clinic every 3-6 months to have a check-up and cystoscopy. If the cancer has not returned, you will continue receiving your treatment.
Impact	<ul style="list-style-type: none"> You will likely be able to continue all normal daily activities and work. You will travel to the hospital for your appointments and to receive treatment during the working week, which might affect your work or personal life. You may experience side effects from your experimental treatment such as: bladder spasm, pain or discomfort while peeing, bladder discharge for 1 or 2 days. You may also experience fatigue, urine infection and a sudden, strong need to pee. You may feel anxious that your cancer may return.

Results



Demographic and Clinical Information - Main Study

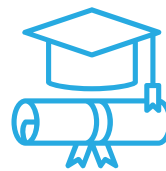


Mean age (SD)
46.0 (14.6) years

Sex at birth: female, N (%)
92 (**45.5%**)

Not married/cohabitating/living with a partner, N (%)
109 (**45.0%**)

Education Level (%) N



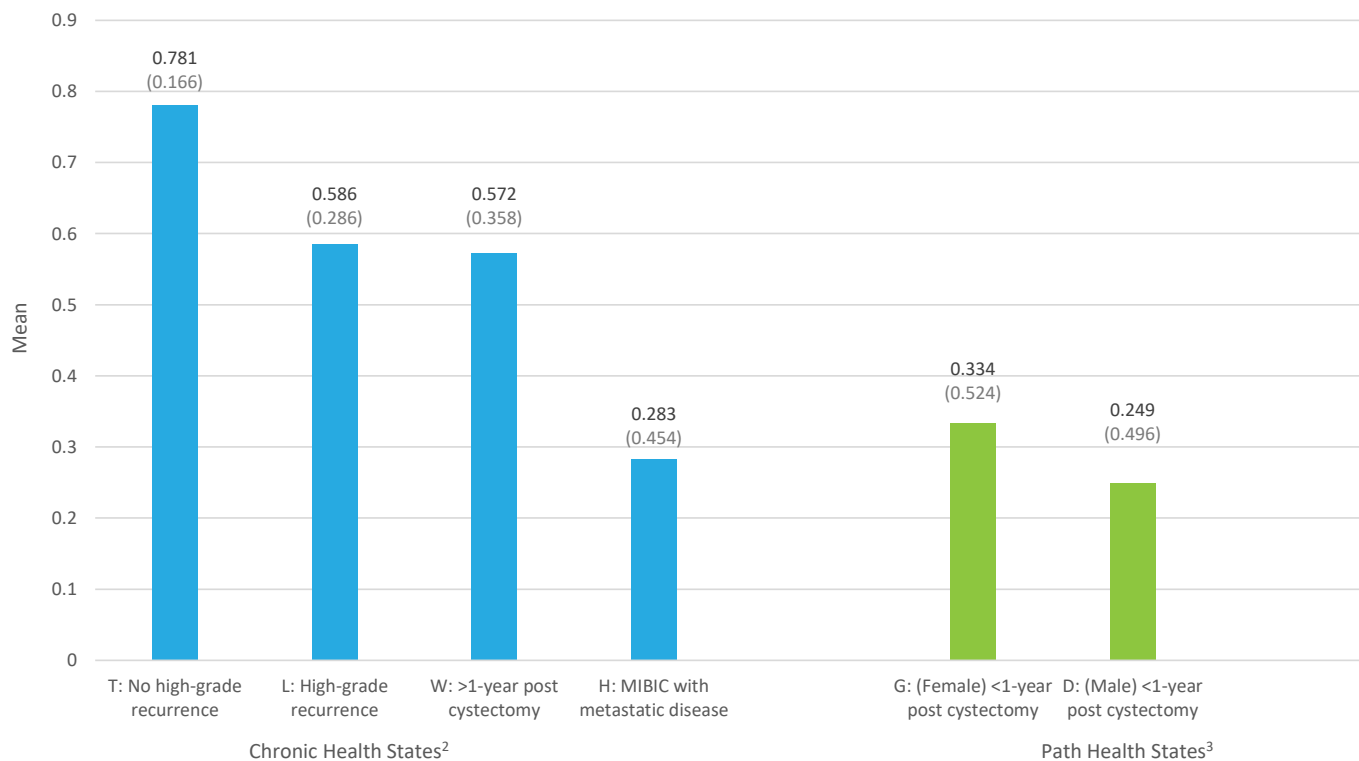
- 40.6%** (n=82) University degree (BA, BSc)
- 21.3%** (n=43) Postgraduate degree (MA, PhD, PGCE)
- 16.3%** (n=33) A' levels or equivalent
- 12.4%** (n=25) Vocational/work-based qualifications
- 8.9%** (n=18) GCSE/O' levels or equivalent

EQ-5D-5L Scores Main Study: Mean (SD)



- 1.20** (0.61) Mobility
- 1.06** (0.37) Self-Care
- 1.14** (0.52) Usual Activities
- 1.38** (0.71) Pain/Discomfort
- 1.40** (0.74) Anxiety/Depression
- 0.89 (0.18) Index Score**
- 83.17** (12.28) VAS

Health State¹ Utility Scores: Main Study (N=202)



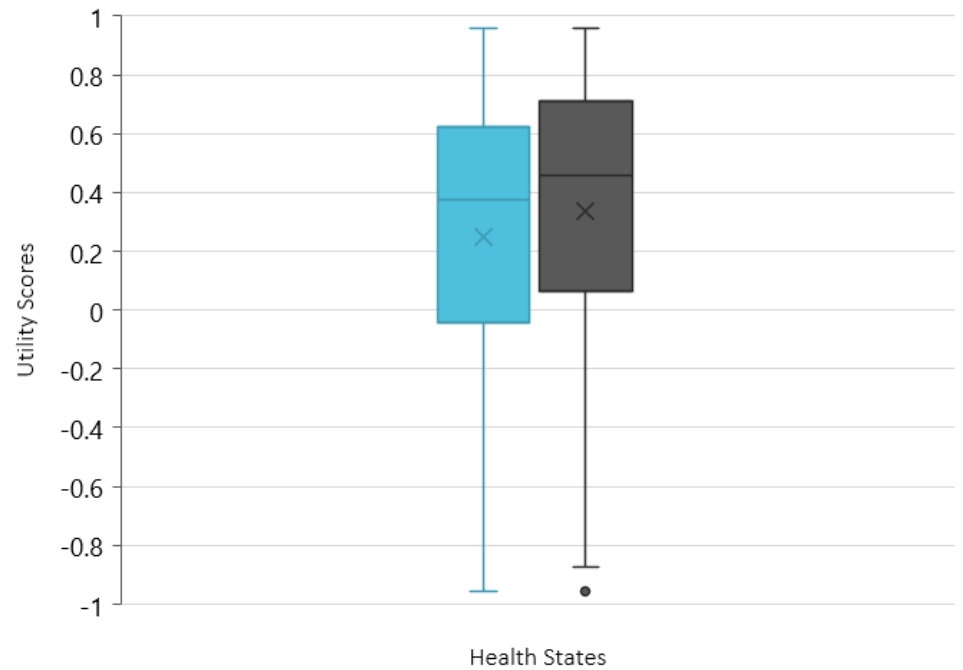
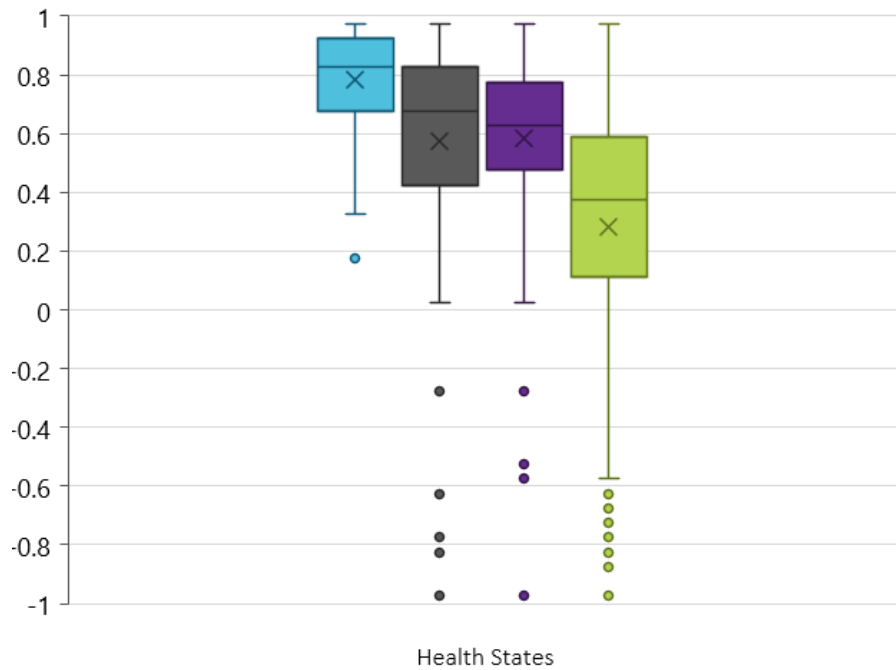
¹ TTO scores are on a scale anchored with 0 representing dead and 1 representing full health.

² A utility of -0.975 is considered to be at the floor. A utility of 0.975 or 1.000 is considered to be at the ceiling.

³ A utility of -0.958 is considered to be at the floor. A utility of 0.958 or 1.000 is considered to be at the ceiling.

The combined D/G score was 0.288 (0.509)

Health State Utility Scores: Main Study (box plot, N=202)



- T: No High-Grade Recurrence
- L: High-Grade Recurrence
- W: >1-year Post Cystectomy
- H: MIBC with Metastatic Disease

- D: First Year Post-Cystectomy (Male)
- G: First Year Post-Cystectomy (Female)

Abbreviation: MIBC = muscle invasive bladder cancer

Willingness to Trade Time: Main Study (N=202)

Health State	Participants willing to trade time ¹ N (%)	Participants not willing to trade time ² N (%)
Chronic Health States		
T: No high-grade recurrence	171 (84.7%)	31 (15.3%)
W: >1-year post cystectomy	196 (97.0%)	6 (3.0%)
L: High-grade recurrence	193 (95.5%)	9 (4.5%)
H: MIBC with metastatic disease	200 (99.0%)	2 (1.0%)
Path Health States		
D: First year post cystectomy (male)	104 (94.5%)	6 (5.5%)
G: First year post cystectomy (female)	89 (96.7%)	3 (3.3%)
D/G: First year post cystectomy	193 (95.5%)	9 (4.5%)

Abbreviation: MIBC = muscle invasive bladder cancer

¹ Participants were considered willing to trade time if the TTO utility score was <0.958 (which is the highest possible utility score when conducting TTO interviews with 5% increments; the participant does not consider the health state to equal to full health).

² Participants were considered unwilling to trade time if the health state TTO utility score was ≥0.958.



Discussion and Conclusion

- Preferences among the health states varied, but utilities generally followed expected patterns—the more severe bladder cancer health states resulted in lower utility scores.
- Health state H: Muscle-Invasive Bladder Cancer with Metastatic Disease had a substantially lower mean utility (0.283) than the utilities of the other chronic health states, highlighting the extreme impact of metastatic bladder cancer on QoL.
- Health state W: One-year post-cystectomy had higher mean utility compared to path health states: <1 –year post cystectomy. In the vignette of HS W patients had recovered significantly from the procedure, adjusted to their new condition, and had a much-improved quality of life.
- Limitations:
 - Previous research suggests that utility scores can vary significantly depending upon the valuation methodology employed.
 - The vignettes required that respondents consider a reasonably large number of impacts which may not be a typical focus for them. This may lead to significantly variability in how the exercise was approached.
 - The use of the different time horizons for the chronic versus path health sates means it is not recommended to compare utility scores between these health states.
- Conclusion: These results demonstrate that the general public highly value delaying radical cystectomy as a treatment alternative for bladder cancer. The health state with bladder-sparing therapy elicited a distinctly higher value compared to the other health states.

References

1. Cancer Research UK. Bladder cancer statistics [Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer#heading-Zero>].
2. Cumberbatch MGK, Jubber I, Black PC, et al. Epidemiology of Bladder Cancer: A Systematic Review and Contemporary Update of Risk Factors in 2018. *Eur Urol*. 2018;74(6):784-795.
3. Urology Care Foundation. Non-muscle invasive bladder cancer [Available from: <https://www.urologyhealth.org/urology-a-z/n/non-muscle-invasive-bladder-cancer>].
4. Noon AP, Albertsen PC, Thomas F, Rosario DJ, Catto JW. Competing mortality in patients diagnosed with bladder cancer: evidence of undertreatment in the elderly and female patients. *Br J Cancer*. 2013 Apr 16;108(7):1534-40.
5. Babaian KN, Adams PG, McClure C, Tompkins B, McMurray M. Bacillus calmette-guérin immunotherapy for bladder cancer overview of BCG immunotherapy 2020 [Available from: <https://emedicine.medscape.com/article/1950803-overview>].
6. European Association of Urology. Non-muscle-invasive bladder cancer 2021 [Available from: https://uroweb.org/guideline/non-muscle-invasive-bladder-cancer/#7_4].
7. Rayn KN, Hale GR, Grave GP, Agarwal PK. New therapies in nonmuscle invasive bladder cancer treatment. *Indian J Urol*. 2018;34(1):11-9.
8. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of life research*. 2011 Dec;20(10):1727-36.

Thank you



FERRING

PHARMACEUTICALS