

Patient perception of high-risk non-muscle-invasive bladder cancer: Treatment burden and sex-specific differences

Andrea Kokorovic¹, Wassim Kassouf², Nimira S. Alimohamed³, Peter C. Black⁴, Girish S. Kulkarni⁵, Normand Blais⁶, Aly Khan A. Lalani⁷, Srikala S. Sridhar⁸, Mia Unsworth⁹, Emilia Biondi⁹, Jacob Skilling⁹, Brendan Osborne¹⁰, Marie Deault-Bonin¹⁰, Christopher J. D. Wallis¹¹

¹Department of Urology, Dalhousie University, Halifax, NS, Canada; ²Department of Surgery (Urology), McGill University Health Center, Montreal, QC, Canada; ³Department of Medicine, Division of Medical Oncology, Arthur JE Child Comprehensive Cancer Centre, University of Calgary, Calgary, AB, Canada; ⁴Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada; ⁵Divisions of Urology and Surgical Oncology, Department of Surgery, University Health Network, University of Toronto, Toronto, ON, Canada; ⁶Division of Medical Oncology and Hematology, Department of Medicine, Centre Hospitalier de l'Université de Montréal; Université de Montréal, Montreal, QC, Canada; ⁷Department of Oncology, Juravinski Cancer Centre, McMaster University, Hamilton, ON, Canada; ⁸Division of Medical Oncology, University of Toronto, Princess Margaret Cancer Centre, Toronto, ON, Canada; ⁹Adelphi Real World, Bollington, United Kingdom; ¹⁰Johnson & Johnson, Toronto, ON, Canada; ¹¹Division of Urology, Department of Surgery, University of Toronto; Mount Sinai Hospital; Department of Surgical Oncology, University Health Network, Toronto, ON, Canada

Cite as: Kokorovic A, Kassouf W, Alimohamed NS, et al. Patient perception of high-risk non-muscle-invasive bladder cancer: Treatment burden and sex-specific differences. *Can Urol Assoc J* 2026 October 19; Epub ahead of print <http://dx.doi.org/10.5489/cuaj.9844>

Published online October 19, 2026

Corresponding author: Dr. Andrea Kokorovic, ¹Department of Urology, Dalhousie University, Halifax, NS, Canada; akokorovic@gmail.com

ABSTRACT

Introduction: Patients with high-risk non-muscle-invasive bladder cancer (HR-NMIBC) often experience significant emotional distress related to the ongoing demands of disease management, including treatment-related adverse events, and concerns about disease recurrence or progression. This study assessed real-world emotional, physical, and socioeconomic burden of HR-NMIBC in Canada, and explored sex-specific differences.

KEY MESSAGES

- This study provides a comprehensive understanding of the experience of patients in Canada living with HR-NMIBC beyond clinical outcomes, encompassing the broader physical, emotional, and socioeconomic burden of managing a chronic, recurrent condition.
- We identified gaps between physician and patient perceptions of treatment burden, symptom impact, and BCG tolerability, highlighting a need for systematic integration of patient experience into clinical practice.
- Routine assessment of QoL should be considered an integral part of HR-NMIBC management.
- Embedding patient perspectives and equity considerations into treatment planning and survivorship frameworks is crucial for improving both QoL and long-term outcomes.

Methods: A cross-sectional survey collected data from physicians who were selected based on actively managing HR-NMIBC patients and patients with HR-NMIBC in Canada. Data included symptoms at diagnosis, treatment experience, patient-reported outcomes (PROs), and sex-specific differences on treatment.

Results: Twenty-one physicians provided chart-review data for 126 HR-NMIBC patients (92 male, 34 female). PRO data were available for 78 patients (seven of whom had corresponding physician records and 71 who were obtained separately through Bladder Cancer Canada). Patients reported a broader range and higher prevalence of symptoms at diagnosis than physicians documented, notably nocturia (32% vs. 7%), bladder pain (13% vs. 1%), and fatigue (27% vs. 5%). Bacillus Calmette-Guérin (BCG) was the most common first-line treatment (62%), yet 22% of patients were dissatisfied overall, and 19% found it poorly tolerable. Patients reported significant logistical strain from frequent consultations, as well as emotional distress, including anxiety and depression. Women reported more urinary symptoms (e.g., nocturia: 50% vs. 25%, $p=0.0273$), and experienced greater employment disruption (24% vs. 10%) and caregiver needs (32 vs. 14 hours/week) than men.

Conclusions: HR-NMIBC imposes significant physical, emotional, and socioeconomic burdens, with notable discrepancies between physician and patient perceptions of symptoms and treatment impact. Sex-specific differences highlight the need for tailored patient-centered care strategies.

INTRODUCTION

Bladder cancer ranks among the ten most common cancers worldwide.¹ Approximately 75% of cases present as non-muscle-invasive bladder cancer (NMIBC), which is confined to the urothelial lining of the bladder (stages Ta, T1, and carcinoma in situ [CIS]).² High-risk NMIBC (HR-NMIBC) is defined as the presence of high grade (HG) T1 tumors, recurrent HG Ta or HG Ta tumors >3cm, CIS, BCG failure, variant histology, or HG prostatic urethral involvement³ and represents approximately one-quarter of all NMIBC cases.⁴ NMIBC has a two-thirds risk of recurrence and a 20% risk of progression to muscle-invasive bladder cancer (MIBC), despite treatment.⁵ As MIBC is associated with poor survival, prevention of progression to this entity remains a priority in managing NMIBC.⁶

The standard of care for HR-NMIBC includes transurethral resection of the bladder tumor (TURBT) to resect all visible tumors followed by intravesical bacillus Calmette-Guérin (BCG) therapy.⁷ This treatment is effective but imposes a substantial burden on patients, requiring repeated procedures, instillations and, in some cases, lifelong surveillance. These interventions are also associated with a multitude of potential adverse events, including bleeding, urinary tract infection, pain/dysuria, bothersome lower urinary tract symptoms and, in rare cases, bladder perforation during TURBT.⁸⁻¹⁰ Despite adequate BCG treatment, up to 40% of high-risk patients experience recurrence within five years and require further treatments, including alternative intravesical therapies or radical cystectomy.⁷

Although bladder cancer is approximately three times more common in men than in women, women often present with more advanced disease and experience worse outcomes,

likely due to biological sex differences and delayed diagnosis.^{11,12} While some studies suggest greater recurrence risk in women,^{13,14} sex-specific differences in response to BCG remain inconclusive,¹⁵ with other studies reporting no significant differences in oncologic outcomes.¹⁶

Although BCG therapy has transformed the management of NMIBC, it remains associated with a substantial treatment burden. Despite its effectiveness, patients may experience frequent recurrence, risk of progression, and adverse effects which can lead to treatment discontinuation.^{8,17-19} The need for repeated instillations, long-term surveillance, and frequent TURBT procedures contributes to NMIBC being one of the costliest malignancies to manage.²⁰ A systematic literature review of NMIBC survivors⁸ reported that life-long surveillance and frequent treatments negatively impact patients' physical and mental health-related quality of life.²¹ Fear of disease progression during NMIBC treatment remains a significant psychological burden.²¹

Understanding patients' perspectives of their journey with NMIBC is a crucial first step in improving overall care for patients with this disease. This study addresses this gap by exploring real-world treatment patterns, patient-reported outcomes (PROs), and sex-specific differences among individuals living with HR-NMIBC in Canada.

Aim of the study

The objective of this study was to assess real-world emotional, physical, and socio-economic burdens of HR-NMIBC in Canada from both patient and physician perspectives to inform more patient-centred care and improve adherence to clinical guidelines.

METHODS

Study design

The Adelphi Real-World HR-NMIBC Disease Specific Program™ (DSP) is a cross-sectional survey with retrospective elements that was conducted in Canada between September 2023 and July 2024, used to capture physician and patient perspective of HR-NMIBC. The DSP methodology has been previously described, validated and shown to be representative and consistent over time.^{22,23} The survey included urologists and medical oncologists actively managing patients with HR-NMIBC. Eligible physicians were urologists or medical oncologists directly responsible for treatment decisions and the management of at least six patients with bladder cancer per month. Each participating physician completed a screening questionnaire to document their perceptions and attitudes toward HR-NMIBC management. Physicians were instructed to complete patient-reported forms (PRFs) for up to eight consecutive HR-NMIBC patients based on medical record review and clinical judgment, reflecting routine clinical practice. PRFs collected data on patients' demographics, clinical characteristics, comorbidities, symptoms, treatment history, outcomes, and reasons for treatment selection or discontinuation. Eligible patients were adults (≥ 18 years) with a diagnosis of HR-NMIBC as defined by Canadian Urological Association (CUA) criteria (see Appendix) at least 12 months prior to data collected and were not involved in clinical trials.

Collection of patient reported outcome (PRO) data: Patients whose clinical information was provided by participating physicians were invited to complete a paper

patient self-completion questionnaire (PSC). Seven patients completed the PSC, which captured information on the symptoms experienced, disease impact on daily functioning, and treatment satisfaction over the prior four weeks. Patients were also encouraged to complete the EQ-5D-5L, a validated PRO that assesses general health status across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.²⁴⁻²⁶ An additional 71 patients were recruited separately through Bladder Cancer Canada (BCC). These patients did not have corresponding physician-reported records and completed an electronic patient self-completion questionnaire (ePSC) that included details of treatment administration burden, lost productivity, need for caregiver support, and impact on quality of life. Together, these 78 patients provided the PRO data used in the study. Data analysis

The data analyses were descriptive. Continuous variables were expressed as means and standard deviations (SD) or medians and interquartile ranges (IQR), while categorical variables were summarized by frequencies and proportions. For group comparisons, Fisher's exact test, the Mann Whitney U test, the chi-square (χ^2) test, or Kruskal-Wallis test were used, as appropriate. Missing data were not imputed; sample sizes vary by variable. Analyses were performed using IBM® SPSS® Data Collection Survey Reporter Version 7.5.1 or later (International Business Machines Corp., New York, USA). Bivariate analyses were performed to assess sex-specific differences.

Unless otherwise specified, analyses were based on available response; denominators therefore may vary across outcomes.

Ethical considerations

The DSP complies with all relevant market research guidelines and legal requirements. Only retrospective, de-identified data were collected. The protocol was reviewed by the Pearl Institutional Review Board and deemed exempt from ethical approval (protocol number AG9392). The DSP adheres to European Pharmaceutical Marketing Research Association guidelines²⁷ and applicable legislation, including the US Health Insurance Portability and Accountability Act 1996²⁸ and Health Information Technology for Economic and Clinical Health Act legislation.²⁹

RESULTS

Patient demographics and clinical characteristics

Twenty-one physicians (20 urologists (8 academic, 12 community-based), and 1 community-based medical oncologist) provided data for 126 patients with HR-NMIBC. The median patient age was 73 years (range: 45-88), 73% were men, 90% were white, and 70% were current or former-smokers (Table 1) and most patients were retired (59%). At data collection, 44% had an Eastern Cooperative Oncology Group (ECOG) performance status of 1 or 2. All patients had a Charlson Comorbidities Index (CCI) ≥ 2 , with 38% scoring ≥ 3 . Common comorbidities included diabetes (23%), chronic obstructive pulmonary disease (COPD) (22%), and renal disease (11%).

At diagnosis, 53% of the patients had multifocal tumors, 78% had pure urothelial histology and the most common tumor type was T1 high-grade ($> 3\text{cm}$; 32%; **Error! Reference source not found.**). Physicians ranked that their most important treatment goals

for HR-NMIBC patients were achieving a complete response (43%), extending overall survival (24%), delaying progression to muscle-invasive disease (19%), and delaying recurrence of HR-NMIBC (10%).

Treatment patterns

Following initial diagnosis, 63% (79/126) of patients received one TURBT, 23% (29/126) received more than one TURBT, and 14% (18/126) received no surgery at first line. No patient received radical cystectomy at first line or later line of therapy. Single-dose perioperative chemotherapy was administered to approximately one quarter of patients (mitomycin C 13%; gemcitabine 10%) following TURBT. First-line therapy management included BCG therapy (62%, 79/126), intravesical chemotherapy (6%, 8/126), TURBT only (27%, 34/126), other intravesical treatment (2%, 3/126) or unknown/ no treatment (2%, 2/126; Figure 1) following TURBT. Among those who received BCG at 1L (n=79), 42% received BCG induction only (33/79), 57% received BCG induction and maintenance (45/79), and 1% received chemotherapy induction and BCG maintenance (1/79).

Patient-reported outcomes

Patient experience with BCG therapy

Only 22% of patients reported no complaints about their BCG treatment (Figure 2). The common complaints that patients described with BCG treatment included pain or discomfort during or after treatment (39%), other challenges difficulties or inconveniences with BCG treatment (16%), catheterization for each instillation (16%) and retaining BCG in the bladder (16%), bathroom sanitation requirements (6%), and coping with the dosing frequency (4%). Among the BCG-treated patients (n=69; Figure 3), 22% reported feeling very dissatisfied or dissatisfied, and 19% rated the treatment as ‘not at all’ or ‘slightly’ tolerable.

Patient-reported health-related quality of life (EQ-5D-5L)

Health-related quality of life was assessed using the EQ-5D-5L instrument, which evaluates five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Overall, 20% of patients reported slight or moderate problems with their mobility (Figure 4), while one third of patients reported slight pain or discomfort, and 57% reported slight or moderate anxiety/ depression.

Socioeconomic and time burdens of HR-NMIBC management

Patients attended frequent consultations, with a median interval of 16 weeks (IQR: 12-26) between appointments, a median travel time of 30 (IQR: 20-60) minutes, and a median treatment time of 60 (IQR: 20-60) minutes (Table 3). This time commitment was found to be somewhat to extremely burdensome by 43% of patients. HR-NMIBC impacted employment for 15% of patients, and almost one quarter (23%, 18/78) required caregiver support (Table 3).

Patient vs. physician bladder cancer symptom perspective

Physician-recorded symptoms at diagnosis were compared with patients’ recollection of the symptoms they experienced at diagnosis. These comparisons were made between groups and

did not represent matched physician and patient reports for the same individuals. Hence, observed differences may reflect variations in patient demographics, timing of data collection, and patient recall. With these limitation in mind, patients reported a broader range and higher prevalence of symptoms than were documented by physicians. The largest differences in perspective were for nocturia (32% vs 7%), bladder pain (13% vs 1%), frequent need to urinate (37% vs 25%), and fatigue (27% vs 5%) (Figure 5).

Sex-specific differences

The majority of males were current or former-smokers (75%) compared to just over half of females with HR-NMIBC (59%) (Table 1). A greater proportion of women than men had an ECOG performance status score of 1 or 2 (59% vs 38%, respectively, $p=0.0563$). A CCI score of 2 was found to be similar in both males and females (64% vs 56%, respectively) and myocardial infarction was more frequent in men than in women (13% and 6%, respectively, $p=0.3485$). Employment (full- or part-time) was more common in men than in women (34% and 9%, respectively, $p=0.0029$).

At diagnosis, 71% of females had multifocal tumors compared to 47% of males (Table 2). The most common tumor type in both males and females was T1 high-grade ($> 3\text{cm}$; both 32%). Women had a higher rate of CIS + T1 and multifocal disease compared to men (35% vs 10% respectively).

Patient experience with BCG therapy also varied; a greater proportion of women were 'very dissatisfied' (16%) and reported that BCG was 'not at all tolerable' (20%) compared to men (9% and 7%, respectively; Figure 3). The common complaints that male and female patients described with BCG treatment included pain or discomfort during or after treatment (48% of men and 24% of women), other challenges, difficulties or inconveniences with BCG treatment, catheterization for each instillation and retaining BCG in the bladder (both 16%), bathroom sanitation requirements (5% of men and 8% of women), and coping with the dosing frequency (5% of men and 4% of women).

A greater percentage of men reported problems with self-care (12% vs 0%; $p=0.0514$) and moderate/severe problem in usual activities (10% vs 3%, $p=0.3069$), and pain/discomfort (14% vs 7%, $p=0.4829$) than women (Figure 4). A higher percentage of women reported anxiety/depression compared to men (24% vs 12%, $p=0.5792$). Socioeconomic impact was also disproportionately higher among women, who were more likely to experience employment disruption (24% vs 10% respectively) and required greater caregiver support (mean [SD] 32.1 [61.5] vs 13.6 [28.9] hours per week).

When symptoms reported by women were compared with those reported by men, a greater percentage of women reported HR-NMIBC-related symptoms than men, particularly nocturia (50% vs 25%, $p=0.0273$). A greater percentage of men (41%) reported experiencing fatigue than women did (18%), $p<0.05$ (Figure 6).

DISCUSSION

This study provides a comprehensive understanding of the experience of patients living with HR-NMIBC, extending beyond clinical outcomes, to encompass the broader physical, emotional, and socioeconomic burden of managing a chronic, recurrent condition. The typical HR-NMIBC patient is older (≥ 70 years) and often has multiple comorbidities, which

complicate treatment decisions and increase vulnerability to both disease progression and treatment-related side effects.

The management of HR-NMIBC is intensive and involves repeated interventions such as TURBT, intravesical therapy (commonly BCG), and frequent cystoscopic surveillance. These demands impose significant logistical and psychosocial strain, particularly for patients balancing employment, caregiving roles, or other responsibilities. Despite NMIBC being the most common form of bladder cancer, studies on its long-term impact on patient quality of life are limited.³⁰ Our study contributes to the growing body of evidence regarding the consequences of HR-NMIBC treatment on patients' quality of life. Nearly one-quarter of patients in our study required additional caregiver support, underscoring the ripple effect on families and support networks. Patient experience is becoming increasingly recognized as a fundamental dimension of cancer care quality.^{34,35} A large-scale UK survey revealed persistent disparities in patient-reported experiences, particularly among younger and older patients, ethnic minorities, and -albeit to a lesser extent - women.³⁵ These differences were attributed to disease-specific factors such as diagnosis delays, treatment burden, and prognosis. Our findings support the importance of patient-centered approaches in HR-NMIBC, especially for those navigating complex treatment pathways or facing uncertain prognoses.

Patients reported more frequently urinary symptoms, pain and fatigue at the time of diagnosis than were documented by physicians, suggesting potential perceptions difference in symptom burden and underscoring the value of incorporating PROs in clinical practice. These findings should be interpreted cautiously. Comparisons between physician and patient reported symptoms were exploratory and limited by the relatively small cohorts. In addition, patient-reported outcomes were collected at a single time point and may have been influenced by recall bias, particularly among patients with more remote diagnoses or treatment experiences. PROs were optional, resulting in variable sample sizes across measures. The majority of PRO data were provided by the BCC cohort, for whom detailed demographic, clinical data, and no prior treatment specified were not specified. As a result, this cohort may have been a heterogeneous group, and comparisons with the physician-reported cohort should be interpreted with caution.

Sex-specific disparities in bladder cancer are well-established,¹⁵ with women often presenting with more advanced disease and experiencing poorer outcomes than men.^{11,31} Evidence suggests reduced effectiveness of intravesical BCG and higher recurrence rates in female patients with NMIBC, as well as increased cancer-specific mortality following radical cystectomy.^{32,33} Despite these clinical differences, real-world data on the sex-specific experience of HR-NMIBC—particularly its physical, emotional, and socioeconomic impact—remain limited and warrant further investigation. Our study found that patient reported outcomes were comparable across sexes, although women reported more urinary symptoms and less satisfaction with BCG therapy, suggesting a need for tailored counseling and support. Emotional distress—including anxiety and depression—was prevalent and persistent, particularly among women.

However, these observed differences should be interpreted cautiously, as women i had less favorable baseline clinical and disease characteristics, including worse ECOG

performance status, higher comorbidity burden. Some of the observed sex-specific differences may reflect differences in baseline patient and tumor characteristics rather than sex itself. The small sample size, unequal sex distribution, and baseline clinical differences, sex-specific findings should be interpreted as exploratory and hypothesis-generating. Larger studies with sufficient sample size and multivariable adjustment are needed to better determine whether sex independently contributes to differences in treatment experience. The heterogeneous nature of HR-NMIBC symptoms can contribute to a delay in diagnosis. Following diagnosis, many patients are not actively involved in the treatment decision-making process and rely on physicians. This can result in a limited understanding of treatment expectations and their potential consequences. A systematic review of qualitative evidence highlighted the significant emotional toll of bladder cancer on patients and families, who are often overlooked in clinical care.³⁶ Greater emphasis on patient counseling and education may help bridge this gap, empowering patients to participate more meaningfully in their care and improve their level of satisfaction.

There is growing optimism surrounding a number of promising novel intravesical agents, including BCG-based combination therapies, novel chemotherapy-based combinations, immunotherapies, oncolytic virus, and prolonged drug-release systems that have promising response rates and improved PROs in BCG-unresponsive HR-NMIBC patients.⁵ Future treatment strategies should prioritize long-term outcomes, quality of life, and patient-centered measures to better align care with the needs and experiences of individuals living with HR-NMIBC.

Limitations

We acknowledge that this study has several limitations. Its observational design, and reliance on survey-based data, introduce potential selection and reporting biases. Patient eligibility and classification were based on the professional judgment of the participating physicians, which may limit generalizability to the broader Canadian HR-NMIBC population. Only patients actively consulting with their physician during the data collection period were included, potentially overrepresenting individuals with more frequent healthcare interactions. To mitigate selection bias, physicians were instructed to report on a consecutive series of eligible patients.

Interpretation of treatment patterns should be made cautiously, as treatment data were derived from physician-reported records reflecting routine clinical practice and information available at the time of consultation. Physician participation was voluntary and may have been influenced by individual willingness to complete the survey.

CONCLUSIONS

This large real-world study reveals that survivorship in HR-NMIBC extends beyond tumor control to encompass physical, emotional, and logistical challenges that are often underrecognized in routine care. Meaningful gaps between physician and patient perceptions—particularly regarding treatment burden, symptom impact, and BCG tolerability—highlight the need for systematic integration of patient voice into clinical practice. Notably, sex-specific differences in experiences reveal distinct needs that warrant consideration in future interventions, guideline development and educational initiatives. By

embedding patient perspectives and equity considerations into treatment planning and survivorship frameworks, we can advance truly patient-centered care and improve both quality of life and long-term outcomes for individuals living with HR-NMIBC.

DRAFT

REFERENCES

1. Richters A, Aben KKH, Kiemeny L. The global burden of urinary bladder cancer: An update. *World J Urol* 2020;38:1895-904. <https://doi.org/10.1007/s00345-019-02984-4>
2. Filon M, Schmidt B. New treatment options for non-muscle-invasive bladder cancer. *Am Soc Clin Oncol Educ Book* 2025;45:e471942. <https://doi.org/10.1200/edbk-25-471942>
3. Matulewicz RS, Steinberg GD. Non-muscle-invasive bladder cancer: Overview and contemporary treatment landscape of neoadjuvant chemoablative therapies. *Rev Urol* 2020;22:43-51.
4. Williams SB, Howard LE, Foster ML, et al. Estimated costs and long-term outcomes of patients with high-risk non-muscle-invasive bladder cancer treated with Bacillus Calmette-Guérin in the Veterans Affairs health system. *JAMA Netw Open* 2021;4:e213800. <https://doi.org/10.1001/jamanetworkopen.2021.3800>
5. Ghodoussipour S, Bivalacqua T, Bryan RT, et al. A systematic review of novel intravesical approaches for the treatment of patients with non-muscle-invasive bladder cancer. *Eur Urol* 2025;88:33-55. <https://doi.org/10.1016/j.eururo.2025.02.010>
6. van den Bosch S, Alfred Witjes J. Long-term cancer-specific survival in patients with high-risk, non-muscle-invasive bladder cancer and tumour progression: A systematic review. *Eur Urol* 2011;60:493-500. <https://doi.org/10.1016/j.eururo.2011.05.045>
7. Bhindi B, Kool R, Kulkarni GS, et al. Canadian Urological Association guideline on the management of non-muscle-invasive bladder cancer - Full-text. *Can Urol Assoc J* 2021;15:E424-60. <https://doi.org/10.5489/cuaj.7367>
8. Jung A, Nielsen ME, Crandell JL, et al. Quality of life in non-muscle-invasive bladder cancer survivors: A systematic review. *Cancer Nurs* 2019;42:E21-33. <https://doi.org/10.1097/ncc.0000000000000606>
9. Jung A, Nielsen ME, Crandell JL, et al. Health-related quality of life among non-muscle-invasive bladder cancer survivors: A population-based study. *BJU Int* 2020;125:38-48. <https://doi.org/10.1111/bju.14888>
10. Rutherford C, Tait MA, Costa DSJ, et al. Development and psychometric evaluation of a patient-reported symptom index for patients with non-muscle invasive bladder cancer: The NMIBC-SI. *J Patient Rep Outcomes* 2025;9:36. <https://doi.org/10.1186/s41687-025-00864-7>
11. Doshi B, Athans SR, Woloszyńska A. Biological differences underlying sex and gender disparities in bladder cancer: Current synopsis and future directions. *Oncogenesis* 2023;12:44. <https://doi.org/10.1038/s41389-023-00489-9>
12. Holzbeierlein JM, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. *J Urol* 2024;211:533-8. <https://doi.org/10.1097/ju.0000000000003846>
13. Schneidewind L, Kiss B, Kranz J, et al. Gender-specific differences in recurrence and progression following Bacillus Calmette-Guérin instillation for non-muscle-invasive bladder cancer. *Urol Int* 2025;109:412-24. <https://doi.org/10.1159/000542473>
14. Schneidewind L, Kiss B, Neumann T, et al. Sex-specific differences in recurrence and progression following cytostatic intravesical chemotherapy for non-muscle invasive urothelial bladder cancer (NMIBC). *J Cancer Res Clin Oncol* 2025;151:59. <https://doi.org/10.1007/s00432-025-06108-x>
15. Chaudhary P, Singha B, Abdel-Hafiz HA, et al. Sex differences in bladder cancer: Understanding biological and clinical implications. *Biol Sex Differ* 2025;16:31. <https://doi.org/10.1186/s13293-025-00715-6>

16. Fadel J, Simonyan D, Fradet V, et al. Analysis of sex-based differences to Bacillus Calmette-Guérin for non-muscle invasive bladder cancer. *Urol Oncol* 2022;40:539.e1-8. <https://doi.org/10.1016/j.urolonc.2022.09.024>
17. Alcorn J, Burton R, Topping A. BCG treatment for bladder cancer, from past to present use. *Int J Urol Nurs* 2015;9:177-86. <https://doi.org/10.1111/ijun.12064>
18. Lidagoster S, Ben-David R, De Leon B, et al. BCG and alternative therapies to BCG therapy for non-muscle-invasive bladder cancer. *Curr Oncol* 2024;31:1063-78. <https://doi.org/10.3390/curroncol31020079>
19. Panach-Navarrete J, Devís-Peiró A, Lloret-Durà MA, et al. Quality of life in patients with non-muscle invasive bladder tumor undergoing adjuvant intravesical treatment. *Actas Urol Esp (Engl Ed)* 2023;47:360-8. <https://doi.org/10.1016/j.acuroe.2023.02.003>
20. Lee LJ, Kwon CS, Forsythe A, et al. Humanistic and economic burden of non-muscle invasive bladder cancer: Results of two systematic literature reviews. *Clinicoecon Outcomes Res* 2020;12:693-709. <https://doi.org/10.2147/ceor.S274951>
21. Beeren I, Klerks NE, Aben KK, et al. Health-related quality of life during the first 4 years after non-muscle-invasive bladder cancer diagnosis: Results of a large multicentre prospective cohort. *Eur Urol Oncol* 2024;7:829-37. <https://doi.org/10.1016/j.euo.2023.11.007>
22. Anderson P, Benford M, Harris N, et al. Real-world physician and patient behaviour across countries: Disease-specific programmes - a means to understand. *Curr Med Res Opin* 2008;24:3063-72. <https://doi.org/10.1185/03007990802457040>
23. Anderson P, Higgins V, Courcy J, et al. Real-world evidence generation from patients, their caregivers and physicians supporting clinical, regulatory and guideline decisions: An update on disease specific programmes. *Curr Med Res Opin* 2023;39:1707-15. <https://doi.org/10.1080/03007995.2023.2279679>
24. Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: Past, present and future. *Appl Health Econ Health Policy* 2017;15:127-37. <https://doi.org/10.1007/s40258-017-0310-5>
25. Janssen MF, Szende A, Cabases J, et al. Population norms for the EQ-5D-3L: A cross-country analysis of population surveys for 20 countries. *Eur J Health Econ* 2019;20:205-16. <https://doi.org/10.1007/s10198-018-0955-5>
26. van Hout B, Janssen MF, Feng YS, et al. Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health* 2012;15:708-15. <https://doi.org/10.1016/j.jval.2012.02.008>
27. EphMA. European Pharmaceutical Market Research Association (EphMRA) code of conduct 2019. 2019. Available at: <http://www.ephmra.org/Code-of-Conduct-Support>. Accessed November 22, 2019.
28. US Department of Health and Human Services. Summary of the HIPAA privacy rule. 2003.
29. US Department of Health and Human Services. HITECH Act enforcement interim final rule. Available at: www.healthit.gov/sites/default/files/hitech_act_excerpt_from_arra_with_index.pdf.
30. Nayak A, Cresswell J, Mariappan P. Quality of life in patients undergoing surveillance for non-muscle invasive bladder cancer-a systematic review. *Transl Androl Urol* 2021;10:2737-49. <https://doi.org/10.21037/tau-20-1333>
31. Radkiewicz C, Edgren G, Johansson ALV, et al. Sex differences in urothelial bladder cancer survival. *Clin Genitourin Cancer* 2020;18:26-34. <https://doi.org/10.1016/j.clgc.2019.10.020>
32. Kluth LA, Rieken M, Xylinas E, et al. Gender-specific differences in clinicopathologic outcomes following radical cystectomy: An international multi-institutional study of

- more than 8000 patients. *Eur Urol* 2014;66:913-9.
<https://doi.org/10.1016/j.eururo.2013.11.040>
33. Uhlig A, Strauss A, Seif Amir Hosseini A, et al. Gender-specific differences in recurrence of non-muscle-invasive bladder cancer: A systematic review and meta-analysis. *Eur Urol Focus* 2018;4:924-36. <https://doi.org/10.1016/j.euf.2017.08.007>
34. Kopenhafer L, Thompson A, Chang J, et al. Patient experience and unmet needs in high-risk nonmuscle-invasive bladder cancer: Insights from qualitative interviews and a cross-sectional survey. *Urol Oncol* 2024;42:70.e1-10.
<https://doi.org/10.1016/j.urolonc.2024.01.013>
35. Saunders CL, Abel GA, Lyratzopoulos G. Inequalities in reported cancer patient experience by socio-demographic characteristic and cancer site: Evidence from respondents to the English Cancer Patient Experience Survey. *Eur J Cancer Care (Engl)* 2015;24:85-98. <https://doi.org/10.1111/ecc.12267>
36. Edmondson AJ, Birtwistle JC, Catto JWF, et al. The patients' experience of a bladder cancer diagnosis: A systematic review of the qualitative evidence. *J Cancer Surviv* 2017;11:453-61. <https://doi.org/10.1007/s11764-017-0603-6>

ACKNOWLEDGEMENTS: Medical writing support (including development of a draft outline and subsequent drafts in consultation with the authors, assembling tables and figures, collating author comments, copy editing, fact checking and referencing) was provided by K Ian Johnson BSc, MBPS, SRPharmS, Harrogate House, Macclesfield, UK and funded by J&J.

FUNDING: Data collection was undertaken by Adelphi Real World (ARW) as part of an independent survey, entitled the ARW High-Risk Non-Muscle Invasive Bladder Cancer (HR-NMIBC) Disease Specific Programme (DSP). Johnson and Johnson Innovative Medicine (Toronto, Ontario, Canada) did not influence the original survey through either contribution to the design of questionnaires or data collection. The analysis described here used data from the ARW HR-NMIBC DSP. The DSP is a wholly owned ARW product. Johnson and Johnson Innovative Medicine (Toronto, Ontario, Canada) is one of multiple subscribers to the DSP. Publication of survey results was not contingent on the subscriber's approval or censorship of the manuscript. Johnson and Johnson Innovative Medicine (Toronto, Ontario, Canada) funded the analysis and development of the publication, including medical writing services. All data, i.e. methodology, materials, data and data analysis, that support the findings of this survey are the intellectual property of Adelphi Real World. All requests for access should be addressed directly to Mia Unsworth at mia.unsworth@omc.com.

DISCLOSURES:

Andrea Kokorovic: Ad boards/speakers bureau: Tolmar, Astellas, Bayer, Ferring, Knight, Pfizer, Tersera, Janssen, EMD Serono, Johnson and Johnson, Astra Zeneca, CG Oncology; Paid travel expenses: Janssen, Tersera.

Wassim Kassouf: Honoraria for ad boards: Ferring, Astra Zeneca, BMS, Merck, Janssen, Bayer, Astellas, Pfizer, EMD Serono, Photocure, CG Oncology, enGene.

Nimira Alimohamed: Advisory board member and received honoraria from EMD Serono, Pfizer, Seagen, Gilead, AstraZeneca, BMS, Merck, Bayer, Astellas, Janssen.

Peter Black: Consulting fees: AbbVie, Astellas, AstraZeneca, Aura, Bayer, BMS, CG Oncology, Combat, EMD-Serono, EnGene, Ferring, Janssen, Merck, Nonagen, Nanology, Nanobot, Pfizer, Photocure, Prokarium, Sumitomo, TerSera, Tolmar, Verity. Speaker: Janssen, TerSera, Bayer, Pfizer. Clinical trials: Janssen, CG Oncology, EnGene, Verity, Therelase, Pacific Edge, Pfizer. Shared patent: Veracyte. Junichi Inokuchi: Honoraria/Travel: Astellas Pharma Inc., ONO Pharmaceutical Co., LTD., Merck & Co., inc.

Gitish Kulkarni: Advisor, consultant, or trial work: Merck, BMS, EMD Serono, Pfizer, Janssen, Ferring, Therelase, Verity, TerSera, Knight Therapeutics, PhotoCure, AstraZeneca.

Normand Blais:

Aly Khan A. Lalani: Astellas Pharma; Bayer; Bristol-Myers Squibb; Eisai; Ipsen; Merck; Novartis; Pfizer; Roche/Genentech. Consulting or Advisory Role - Abbvie; Astellas Pharma; Bayer; Bristol-Myers. Squibb; Eisai; Ipsen; Janssen; Merck; Novartis; Pfizer. Research Funding - BioCanRx (Inst); Bristol-Myers Squibb (Inst); EMD Serono (Inst); Ipsen (Inst); Novartis (Inst); Roche (Inst).

Srikala S. Sridha: Consulting fees: Astellas, AstraZeneca, Bayer, BMS, Eisai, EMD Serono, Hoffmann-La Roche, Immunomedics, Ipsen, Janssen, Merck, Pfizer, Seagen; Honoraria: Bayer, EMD Serono, Pfizer, Seagen; Meeting attendance/travel: EMD Serono.

Jacob Skilling, Emilia Biondi and Mia Unsworth: Employees of Adelphi Real-World, UK.

Brendan Osborne and Marie Deault-Bonin: Employees of Johnson & Johnson and may hold stocks/stock options in Johnson & Johnson.

Christopher Wallis: Consulting Fees: Johnson & Johnson Innovative Medicine, Nanostics Inc, Precision Point Specialty LLC, SESEN Bio; Honoraria/Travel: AbbVie, Astellas, Astra Zeneca, Bayer, EMD Serono, Haymarket Media, Healing and Cancer Foundation, Johnson & Johnson Innovative Medicine, Knight Therapeutics, Intuitive Surgical, MashUP Media, Merck, Pfizer, Science & Medicine Canada, Sumitomo Pharmaceuticals, TerSera Canada, Tolmar Pharmaceuticals Canada; Research Funding: Knight Therapeutics, Tolmar Pharmaceuticals, Bayer, Sunnybrook HSC AFP

FIGURES AND TABLES

Figure 1. Summary of treatment patterns at 1L, 2L, and 3L. BCG: bacillus Calmette-Guérin; IVES chemo: intravesical chemotherapy; 1L: first-line; 2L: second-line; 3L: third-line; TURBT: transurethral resection of bladder tumor.

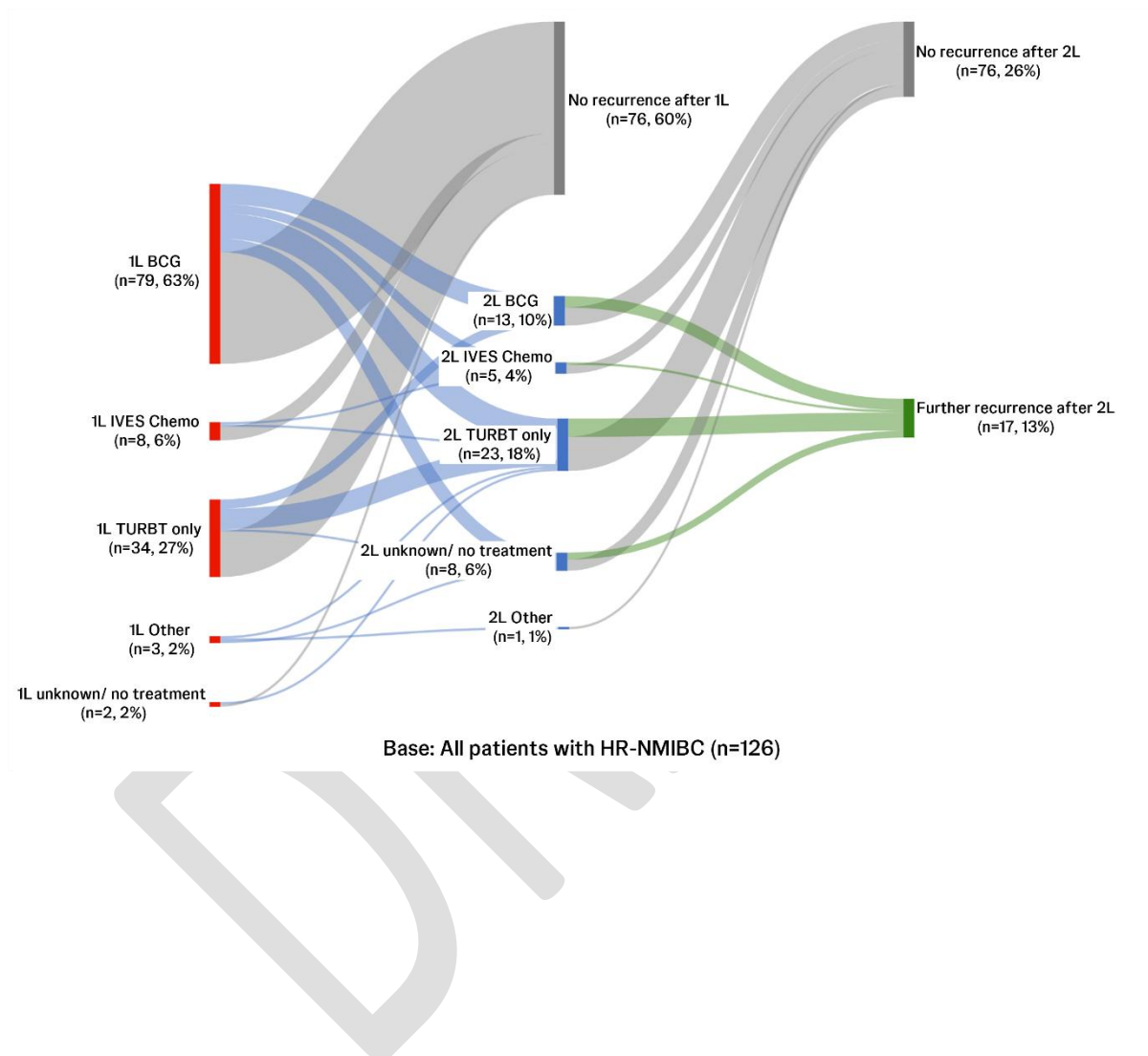
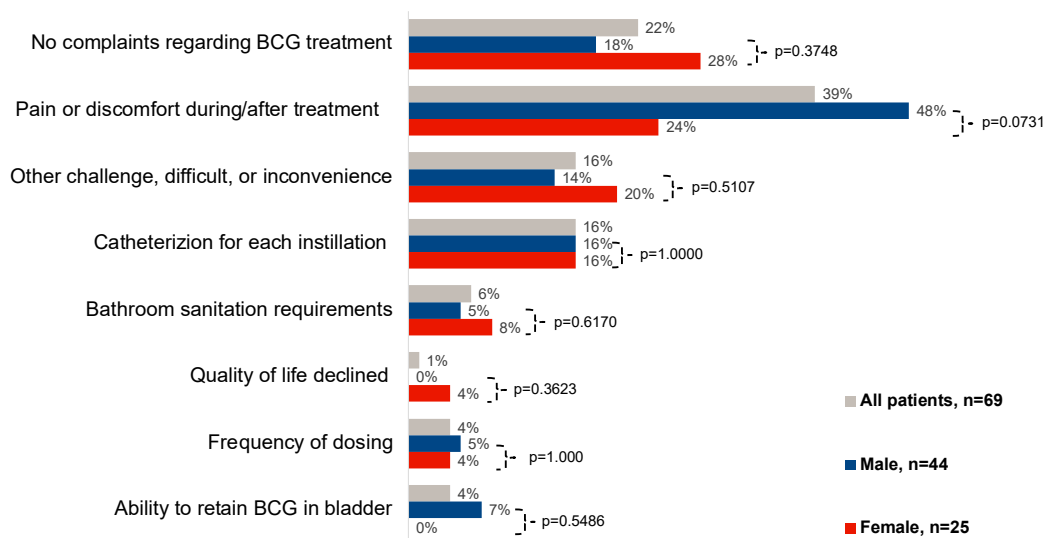
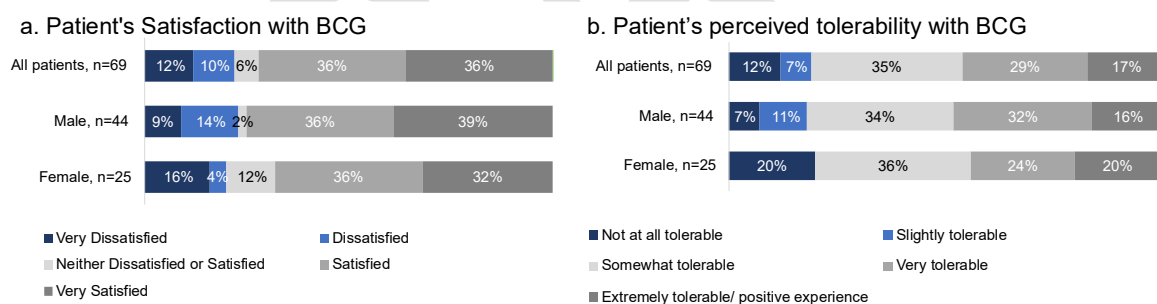
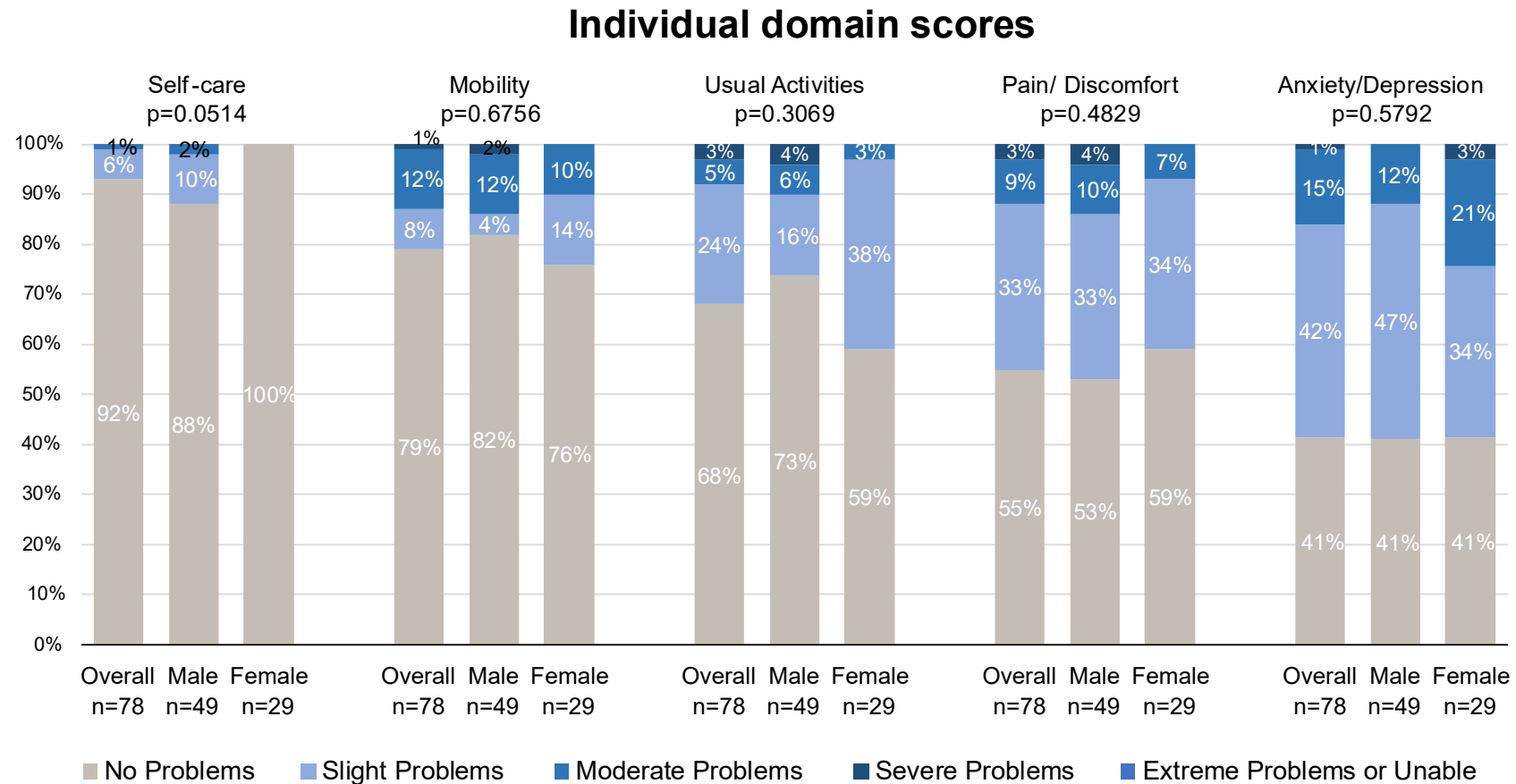


Figure 2. Patients' major complaints about BCG treatment. BCG: bacillus Calmette-Guérin.

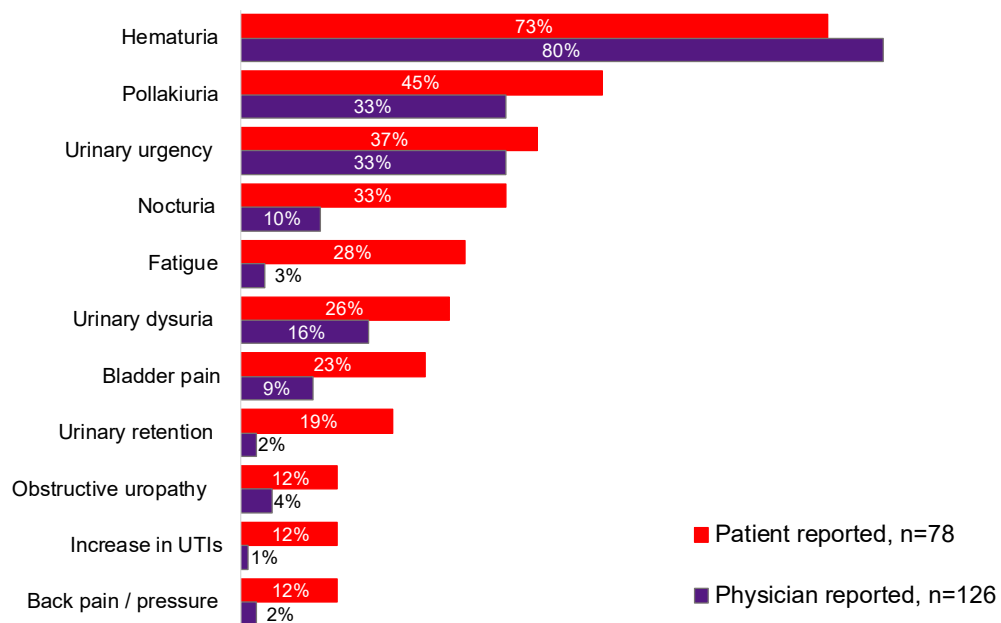
Base: All patients with HRNMIBC who completed a PSC or ePSC, who stated they had received treatment within the past 4 weeks for their NMIBC.

Figure 3. (a) Patients' satisfaction; and (b) perceived tolerability of BCG by sex. BCG: bacillus Calmette-Guérin.

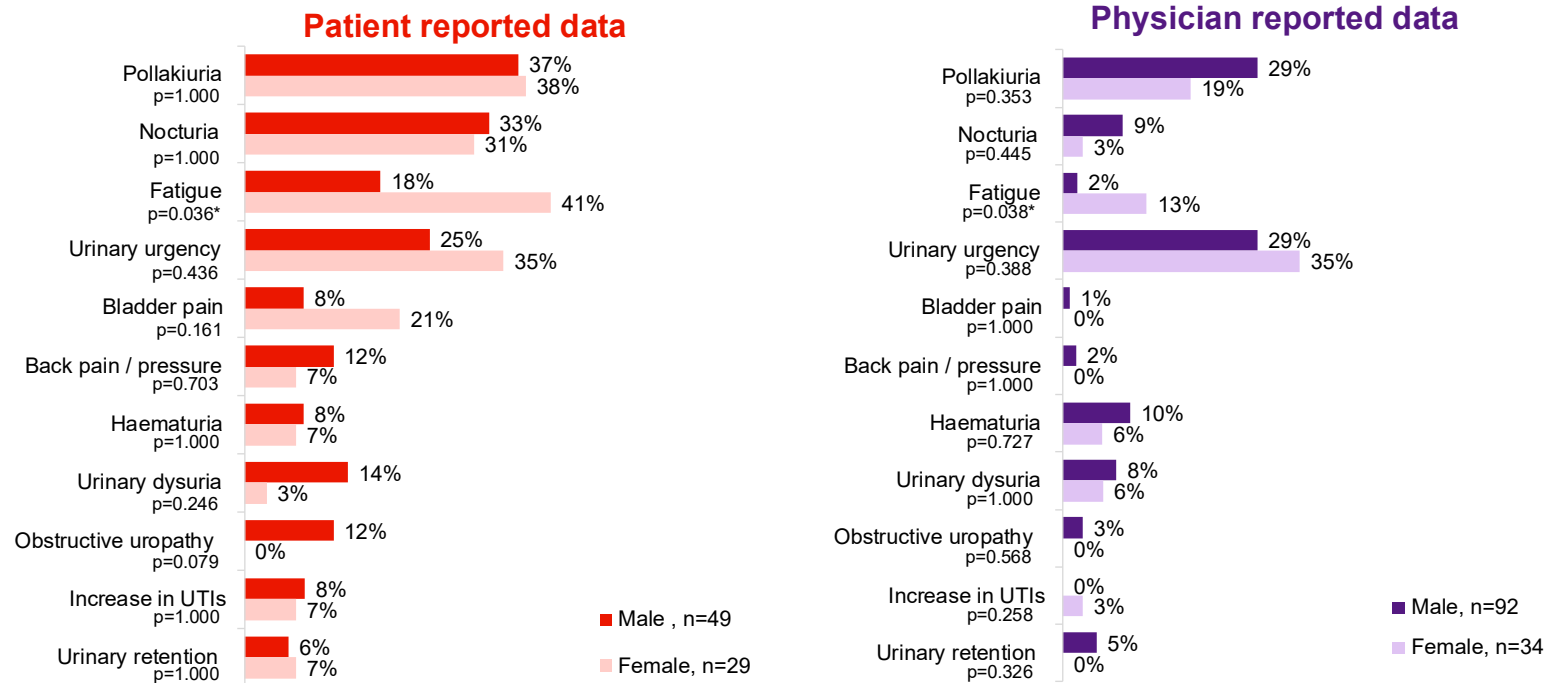
Base: All patients with HR-NMIBC who completed a PSC or ePSC, who stated they had received BCG treatment for their NMIBC.

Figure 4. Impact of high-risk non-muscle-invasive bladder cancer on patients' health-related quality of life (EQ-5D-5L).

Base: All patients with HR-NMIBC who completed a PSC or ePSC (n=78)
 P values are comparing the difference between gender (males vs females) using a Mann-Whitney test.

Figure 5. Patient vs. physician perspective of bladder cancer symptoms at non-muscle-invasive bladder cancer diagnosis.

Base: All patients with HR-NMIBC (n=126) and all patients with HR-NMIBC who completed a PSC or ePSC (n=78)

Figure 6. Patient vs. physician perspective of bladder-related symptoms by sex

Base: Symptoms recalled by patients with HR -NIMBC who completed a PSC or ePSC (n=78) and physician-reported symptoms at diagnosis (n=126). Differences between males and females annotated with an asterisk were significant at the $p < 0.05$ level

Table 1. Patient demographics at data collection

	All patients n=126	Male n=92	Female n=34
Age, median (range)	73 (45–88)	73 (51–88)	72.5 (45–88)
Ethnicity, n (%)			
White	113 (90%)	88 (96%)	25 (74%)
Black	4 (3%)	0 (0%)	4 (12%)
First Nations/Inuit/Métis	2 (2%)	0 (0%)	2 (6%)
American Native	1 (1%)	1 (1%)	0 (0%)
East or Southeast Asian	6 (5%)	3 (3%)	3 (9%)
Middle Eastern or North African	2 (2%)	0 (0%)	2 (6%)
Smoking status, n (%)			
Current smoker	17 (13%)	12 (13%)	5 (15%)
Ex-smoker	72 (57%)	57 (62%)	15 (44%)
Never smoked	25 (20%)	15 (16%)	10 (29%)
Not known	12 (10%)	8 (9%)	4 (12%)
ECOG score at time of data collection, n (%)			
0	71 (56%)	57 (62%)	14 (41%)
1	50 (40%)	31 (34%)	19 (56%)
2	5 (4%)	4 (4%)	1 (3%)
Charlson Comorbidity Index, n (%)			
2	78 (62%)	59 (64%)	19 (56%)
≥3	48 (38%)	33 (36%)	15 (44%)
Concomitant conditions (>10%), n (%)			
Diabetes	29 (23%)	21 (23%)	8 (24%)
Chronic pulmonary disease	28 (22%)	19 (21%)	9 (26%)
Renal disease	14 (11%)	7 (8%)	7 (21%)
Myocardial infarction	14 (11%)	12 (13%)	2 (6%)
Employment status, n (%)			
Retired	74 (59%)	52 (57%)	22 (65%)
Working full-time	29 (23%)	27 (29%)	2 (6%)
Working part-time	6 (5%)	5 (5%)	1 (3%)
Homemaker	9 (7%)	4 (4%)	5 (15%)
Unemployed	1 (1%)	1 (1%)	0 (0%)
On long-term sick leave	1 (1%)	0 (0%)	1 (3%)
Not known	6 (5%)	3 (3%)	3 (9%)

ECOG: Eastern Cooperative Oncology Group; TURBt: transurethral resection of bladder cancer

Table 2. Baseline tumor characteristics at the time of initial NMIBC diagnosis			
	All patients n=126	Male n=92	Female n=34
Tumor clinical characteristics, n (%)			
Solitary	59 (47%)	49 (53%)	10 (29%)
Multifocal	67 (53%)	43 (47%)	24 (71%)
Histologic differentiation present in urothelial cancer, n (%)			
No histologic variants	98 (78%)	74 (81%)	24 (71%)
Micropapillary	16 (13%)	11 (12%)	5 (15%)
Squamous differentiation	4 (3%)	1 (1%)	3 (9%)
Glandular differentiation	5 (4%)	4 (4%)	1 (3%)
Sarcomatoid	2 (2%)	1 (1%)	1 (3%)
Plasmacytoid	1 (1%)	1 (1%)	0 (0%)
Tumor stage, grade, and size: at the time of initial NMIBC diagnosis, n (%)			
Ta: High-grade / G3 (or high-risk G2) (<3cm)	10 (8%)	8 (9%)	2 (6%)
Ta: High-grade / G3 (or high-risk G2) (>3cm)	12 (9%)	9 (10%)	3 (9%)
T1: Low-grade /G1 or 2 (<3cm)	1 (1%)	1 (1%)	0 (0%)
T1: Low-grade /G1 or 2 (>3cm)	1 (1%)	1 (1%)	0 (0%)
T1: High-grade/G3 (<3cm)	27 (21%)	22 (24%)	5 (15%)
T1: High-grade/G3 (>3cm)	40 (32%)	29 (32%)	11 (32%)
CIS	7 (6%)	6 (6%)	1 (3%)
CIS + Ta HG	7 (6%)	7 (8%)	0 (0%)
CIS + T1	21 (17%)	9 (10%)	12 (35%)

CIS: carcinoma in situ; HG: high-grade; IQR: interquartile range; SD: standard deviation.

Table 3. Treatment administration burden, employment impact and caregiver support

Patient burden	Patients who completed a PSC n=78	Male n=49	Female n=29
Consultations			
Frequency of doctor appointment for NMIBC consultation, median (IQR), weeks	16 (12–26)	16 (12–51)	12 (12–24)
Travel time to NMIBC consultations, median (IQR) minutes	30 (20–60)	30 (20–45)	45 (25–60)
Average travel time to NMIBC treatments, median (IQR), minutes	60 (20–60)	60 (20–60)	60 (30–60)
Duration of treatment administration, n (%)			
Not at all burdensome	12 (33%)	8 (36%)	4 (29%)
Slightly burdensome	9 (25%)	5 (23%)	4 (29%)
Somewhat burdensome	10 (28%)	6 (27%)	4 (29%)
Very burdensome	3 (8%)	2 (9%)	1 (7%)
Extremely burdensome	2 (6%)	1 (5%)	1 (7%)
Change in employment status, n (%)			
No change / not working	66 (85%)	44 (90%)	22 (76%)
Reduced hours	6 (8%)	3 (6%)	3 (10%)
Changed job	3 (4%)	0 (0%)	3 (10%)
Retired	2 (3%)	2 (4%)	0 (0%)
Long-term sick leave	1 (1%)	0 (0%)	1 (3%)
Caregiver support, n (%)			
Additional support received	18 (23%)	11 (22%)	7 (24%)
No additional support	60 (77%)	38 (78%)	22 (76%)
Additional support required weekly, hours			
Mean (SD)	20.8 (43.4)	13.6 (28.9)	32.1 (61.5)

IQR : interquartile range; SD : standard deviation.