Supplementary Online Content

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(3):e213800. doi:10.1001/jamanetworkopen.2021.3800

eFigure 1. Kaplan-Meier Curves for Disease-Free Survival, Overall and Stratified by Clinical Stage Group

eFigure 2. Kaplan-Meier Curves for Time to All-Cause Mortality, Overall and Stratified by Clinical Stage Group

eTable 1. Univariable and Multivariable Association Between Demographic and Disease Characteristics and Disease-Free Survival (n = 401)

eTable 2. Kaplan-Meier Event-Free Survival Estimates From Time of BCG Initiation

eTable 3. Comparisons of Number of Patients With Any Cost vs No Cost Stratified by Progression Status

eTable 4. Association Between Progression Status and Costs (if Any)

eTable 5. Health Care Cost Data From Time of BCG Induction Start Date and 30 and 90 Days After Cystectomy (n = 33)

This supplementary material has been provided by the authors to give readers additional information about their work.
**eFigure 1.** Kaplan-Meier Curves for Disease-Free Survival, Overall and Stratified by Clinical Stage Group
eFigure 2. Kaplan-Meier Curves for Time to All-Cause Mortality, Overall and Stratified by Clinical Stage Group

Kaplan-Meier Curves for Time to All-Cause Mortality, Overall and Stratified by Clinical Stage Group

Number at risk

0 24 48 72 96 120 144 168 192

Months from BCG initiation

Overall survival

Number at risk

CIS ± T1 or TaHG 68 67 63 56 46 41 37 32 27 19 13
TaHG or T1, no CIS 341 330 307 275 230 197 158 121 100 74 63

Months from BCG initiation

Overall survival

log-rank: p=0.32

© 2021 Williams SB et al. JAMA Network Open.
**eTable 1.** Univariable and Multivariable Association Between Demographic and Disease Characteristics and Disease-Free Survival (n = 401)*

|                              | Univariable |          | Multivariable |          |
|------------------------------|-------------|----------|---------------|----------|
|                              | Events/N    | HR (95% CI) | P-value | HR (95% CI) | P-value |
| **Age at BCG initiation**    | 202/401     | 1.01 (0.99-1.02) | 0.20    | 1.00 (0.99-1.02) | 0.69    |
| **Gender**                   |             |          | 0.44    |          | 0.64    |
| Female                       | 33/73       | Ref.     |         | Ref.     |         |
| Male                         | 169/328     | 1.15 (0.80-1.66) | 0.12    | 1.10 (0.75-1.60) | 0.42    |
| **Smoking**                  |             |          | 0.12    |          | 0.22    |
| Current                      | 63/145      | Ref.     |         | Ref.     |         |
| Former                       | 111/199     | 1.37 (1.01-1.85) | 0.08    | 1.25 (0.89-1.76) | 0.57    |
| Never smoker                 | 28/57       | 1.27 (0.82-1.96) |         | 1.20 (0.76-1.91) |         |
| **CIS at High-Risk NMIBC diagnosis** | <0.001 |          |         | <0.001 |
| No                           | 151/333     | Ref.     |         | Ref.     |         |
| Yes                          | 51/68       | 2.14 (1.56-2.94) |         | 1.99 (1.44-2.75) |         |
| **CCI at BCG initiation**    |             | 0.08    |         | 0.22    |
| 0-2                          | 56/112      | Ref.     |         | Ref.     |         |
| 3-4                          | 96/173      | 1.35 (0.97-1.88) |         | 1.21 (0.86-1.70) |         |
| 5+                           | 50/116      | 0.96 (0.66-1.41) |         | 0.90 (0.60-1.35) |         |

BCG= Bacillus Calmette-Guerin; CCI=Charlson comorbidity index; NMIBC=non-muscle invasive bladder cancer

*Patients with BCG initiation prior to 2000 did not have CCI available and were therefore not included in this analysis
**eTable 2. Kaplan-Meier Event-Free Survival Estimates From Time of BCG Initiation**

|                          | 3 years | 5 years | 10 years | 15 years |
|--------------------------|---------|---------|----------|----------|
| **Progression**          |         |         |          |          |
| CIS ± T1 or TaHG         | 88.1%   | 83.5%   | 78.2%    | 73.9%    |
| TaHG or T1, no CIS      | 89.4%   | 86.9%   | 82.2%    | 78.6%    |
| **Cystectomy**          |         |         |          |          |
| CIS ± T1 or TaHG         | 93.0%   | 89.7%   | 88.1%    | 88.1%    |
| TaHG or T1, no CIS      | 94.0%   | 91.8%   | 90.7%    | 90.7%    |
| **Death**                |         |         |          |          |
| CIS ± T1 or TaHG         | 86.6%   | 75.3%   | 52.8%    | 30.5%    |
| TaHG or T1, no CIS      | 86.2%   | 75.7%   | 54.7%    | 36.8%    |
| **BC death**            |         |         |          |          |
| CIS ± T1 or TaHG         | 97.6%   | 94.7%   | 92.15%   | 85.0%    |
| TaHG or T1, no CIS      | 98.5%   | 89.0%   | 86.5%    | -        |

BC=bladder cancer; BCG= Bacillus Calmette-Guerin; CIS=carcinoma in situ
**eTable 3. Comparisons of Number of Patients With Any Cost vs No Cost Stratified by Progression Status**

|                | # (%) cost > $0.00 | P-value<sup>1</sup> | Odds Ratio (95% CI)<sup>2</sup> | P-value<sup>2</sup> |
|----------------|---------------------|----------------------|----------------------------------|----------------------|
|                | No Progression (N=330) | Progression (N=71) |                                  |                      |
| **Total costs**|                     |                      |                                  |                      |
| 1-year         | 303 (92)            | 70 (99)              | 0.040                            | 7.4 (0.8-65.1)       | 0.072               |
| 2-year         | 308 (93)            | 71 (100)             | 0.019                            | NA                   |
| 5-year         | 328 (99)            | 71 (100)             | >0.99                            | NA                   |
| **Inpatient costs** |                     |                      |                                  |                      |
| 1-year         | 54 (16)             | 25 (35)              | <.001                            | 3.2 (1.8-5.8)        | <.001               |
| 2-year         | 78 (24)             | 39 (55)              | <.001                            | 4.3 (2.5-7.5)        | <.001               |
| 5-year         | 143 (43)            | 61 (86)              | <.001                            | 8.2 (4.0-16.6)       | <.001               |
| **Outpatient costs** |                     |                      |                                  |                      |
| 1-year         | 303 (92)            | 70 (99)              | 0.040                            | 7.4 (0.8-65.1)       | 0.072               |
| 2-year         | 308 (93)            | 71 (100)             | 0.019                            | NA                   |
| 5-year         | 328 (99)            | 71 (100)             | >0.99                            | NA                   |
| **Laboratory costs** |                     |                      |                                  |                      |
| 1-year         | 300 (91)            | 68 (96)              | 0.235                            | 2.2 (0.6-8.1)        | 0.255               |
| 2-year         | 307 (93)            | 70 (99)              | 0.096                            | 4.9 (0.6-39.5)       | 0.140               |
| 5-year         | 327 (99)            | 71 (100)             | >0.99                            | NA                   |
| **Pharmacy costs** |                     |                      |                                  |                      |
| 1-year         | 302 (92)            | 67 (94)              | 0.628                            | 1.4 (0.4-5.1)        | 0.635               |
| 2-year         | 308 (93)            | 71 (100)             | 0.019                            | NA                   |
| 5-year         | 328 (99)            | 71 (100)             | >0.99                            | NA                   |
| **Surgery costs** |                     |                      |                                  |                      |
| 1-year         | 187 (57)            | 44 (62)              | 0.430                            | 1.5 (0.9-2.7)        | 0.151               |
| 2-year         | 209 (63)            | 56 (79)              | 0.013                            | 2.8 (1.4-5.4)        | 0.002               |
| 5-year         | 256 (78)            | 68 (96)              | <.001                            | 7.2 (2.2-23.7)       | 0.001               |
| **Radiology costs** |                     |                      |                                  |                      |
|               | Cost (N) | No Cost (N) | P-value | OR (95% CI) | Significance |
|---------------|----------|-------------|---------|-------------|--------------|
| 1-year        | 242 (73) | 57 (80)     | 0.293   | 1.7 (0.9-3.3) | 0.122        |
| 2-year        | 276 (84) | 67 (94)     | 0.024   | 4.0 (1.3-11.9) | 0.014        |
| 5-year        | 311 (94) | 69 (97)     | 0.555   | 2.2 (0.5-10.0) | 0.293        |

1 Fisher’s exact test
2 Odds Ratio of any cost vs. no cost controlling for age at BC diagnosis, race (white, black, other), gender, and year of BC diagnosis
|                      | Median (25th percentile – 75th percentile) |                      |            |            |
|----------------------|------------------------------------------|----------------------|------------|------------|
|                      | No Progression (N=330)                  | Progression (N=71)   | P-value1   | Coefficient2 | P-value2 |
| **Total costs**      |                                          |                      |            |            |
| 1-year               | 29,808 (16,732-50,299)                  | 37,654 (19,550-6,595) | 0.007     | 1.56       | <0.001   |
| 2-year               | 54,422 (29,456-84,264)                  | 104,289 (49,108-18,345) | <.001    | 2.01       | <0.001   |
| 5-year               | 95,565 (52,751-174,119)                 | 233,960 (157,328-346,579) | <.001   | 2.48       | <0.001   |
| **Inpatient costs**  |                                          |                      |            |            |
| 1-year               | 20,232 (7,519-37,148)                   | 53,801 (13,526-85,729) | 0.008     | 2.33       | 0.006    |
| 2-year               | 20,153 (7,719-41,773)                   | 57,002 (21,818-108,524) | <.001    | 2.79       | <0.001   |
| 5-year               | 30,609 (11,116-65,735)                  | 82,824 (52,504-115,695) | <.001   | 2.58       | <0.001   |
| **Outpatient costs** |                                          |                      |            |            |
| 1-year               | 27,936 (16,543-46,480)                  | 34,885 (18,876-72,253) | 0.014     | 1.35       | 0.007    |
| 2-year               | 51,241 (28,700-81,083)                  | 72,323 (49,108-133,648) | <.001    | 1.64       | <0.001   |
| 5-year               | 88,874 (50,130-143,706)                 | 168,379 (113,099-205,709) | <.001   | 1.97       | <0.001   |
| **Laboratory costs** |                                          |                      |            |            |
| 1-year               | 1,152 (562-2,314)                       | 1,932 (870-6,047)    | <.001     | 2.20       | <0.001   |
| 2-year               | 2,151 (1,161-4,062)                     | 4,333 (2,379-11,738)  | <.001     | 2.59       | <0.001   |
| 5-year               | 4,117 (2,109-7,879)                     | 13,279 (6,952-20,123) | <.001    | 2.98       | <0.001   |
| **Pharmacy costs**   |                                          |                      |            |            |
| 1-year               | 2,225 (1,089-4,679)                     | 3,699 (1,437-7,500)  | 0.009     | 1.74       | 0.001    |
| 2-year               | 4,054 (1,796-8,571)                     | 7,536 (2,667-23,308) | <.001     | 1.92       | <0.001   |
| 5-year               | 7,217 (3,653-17,949)                    | 18,306 (10,210-39,045) | <.001   | 2.63       | <0.001   |
| **Surgery costs**    |                                          |                      |            |            |
| 1-year               | 5,955 (2,779-9,688)                     | 11,934 (4,952-34,811) | <.001     | 2.43       | <0.001   |
| 2-year               | 9,645 (4,507-15,778)                    | 18,789 (11,159-40,461) | <.001   | 2.37       | <0.001   |
| 5-year               | 13,813 (6,629-29,161)                   | 34,468 (18,104-67,055) | <.001   | 2.71       | <0.001   |
| **Radiology costs**  |                                          |                      |            |            |
| 1-year               | 822 (383-1,671)                         | 1,144 (418-3,230)    | 0.015     | 1.77       | 0.002    |
| 2-year               | 1,348 (627-2,852)                       | 3,002 (1,230-11,055) | <.001     | 2.84       | <0.001   |
| 5-year               | 2,950 (1,340-5,879)                     | 11,395 (4,990-19,851) | <.001   | 3.75       | <0.001   |

1 Wilcoxon rank sum test
**Table 4.** Association Between Progression Status and Costs (if Any)

|                        | Median (25<sup>th</sup> percentile – 7<sup>th</sup> percentile) | P-value<sup>1</sup> | Coefficient<sup>2</sup> | P-value<sup>2</sup> |
|------------------------|---------------------------------------------------------------|---------------------|---------------------------|---------------------|
| No Progression (N=330) |                                                               |                     |                           |                     |
| Progression (N=71)     |                                                               |                     |                           |                     |

<sup>2</sup> General linear regression on the logarithm of the costs controlling for age at BC diagnosis, race (white, black, other), gender, and year of BC diagnosis. The coefficient of progression relative to no progression was the exponential estimate of the logarithm of the costs.
**eTable 5. Health Care Cost Data From Time of BCG Induction Start Date and 30 and 90 Days After Cystectomy (n = 33)**

| Age at BC diagnosis | 66 (61, 74) |
|---------------------|-------------|
| Race                |             |
| Black               | 2 (6%)      |
| White               | 30 (91%)    |
| Other               | 1 (3%)      |
| Ethnicity           |             |
| Hispanic/Latino     | 1 (3%)      |
| Not Hispanic/Latino | 32 (97%)    |
| Gender              |             |
| Female              | 10 (30%)    |
| Male                | 23 (70%)    |
| Year of BC diagnosis| 2010 (2007, 2013) |

| Costs in USD | From BCG start to follow-up | 30 days post cystectomy | 90 days post cystectomy |
|--------------|-----------------------------|-------------------------|-------------------------|
| Total costs  | 358,593 (257,699, 652,853)  | 89,131 (66,892, 117,921) | 89,889 (72,497, 127,960) |
| Inpatient costs | 101,768 (69,755, 195,203)  | 63,441 (53,801, 84,544)  | -                       |
| Outpatient costs | 235,083 (179,086, 440,244) | 15,218 (7,264, 31,642)  | 26,397 (11,577, 39,253) |
| Laboratory costs | 18,468 (11,529, 27,835)    | 7,367 (4,537, 10,888)   | 7,495 (4,563, 10,888)   |
| Pharmacy costs   | 32,933 (16,532, 68,596)     | 5,107 (3,477, 13,075)   | 5,993 (4,171, 18,897)   |
| Surgery costs    | 76,184 (48,560, 118,196)    | 30,626 (24,064, 49,176) | -                       |
| Radiology costs  | 16,758 (12,322, 39,229)     | 1,726 (417, 4,537)      | 2,130 (1,196, 5,922)    |

BC=bladder cancer; BCG= Bacillus Calmette-Guerin; USD: United States Dollar

All costs are adjusted to 2019 USD using the medical component of the Consumer Price Index (mCPI)

Summary statistics for continuous variables display median (25<sup>th</sup> percentile, 75<sup>th</sup> percentile)

*Six patients who received their cystectomy outside of the VA were not included in this table*