

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

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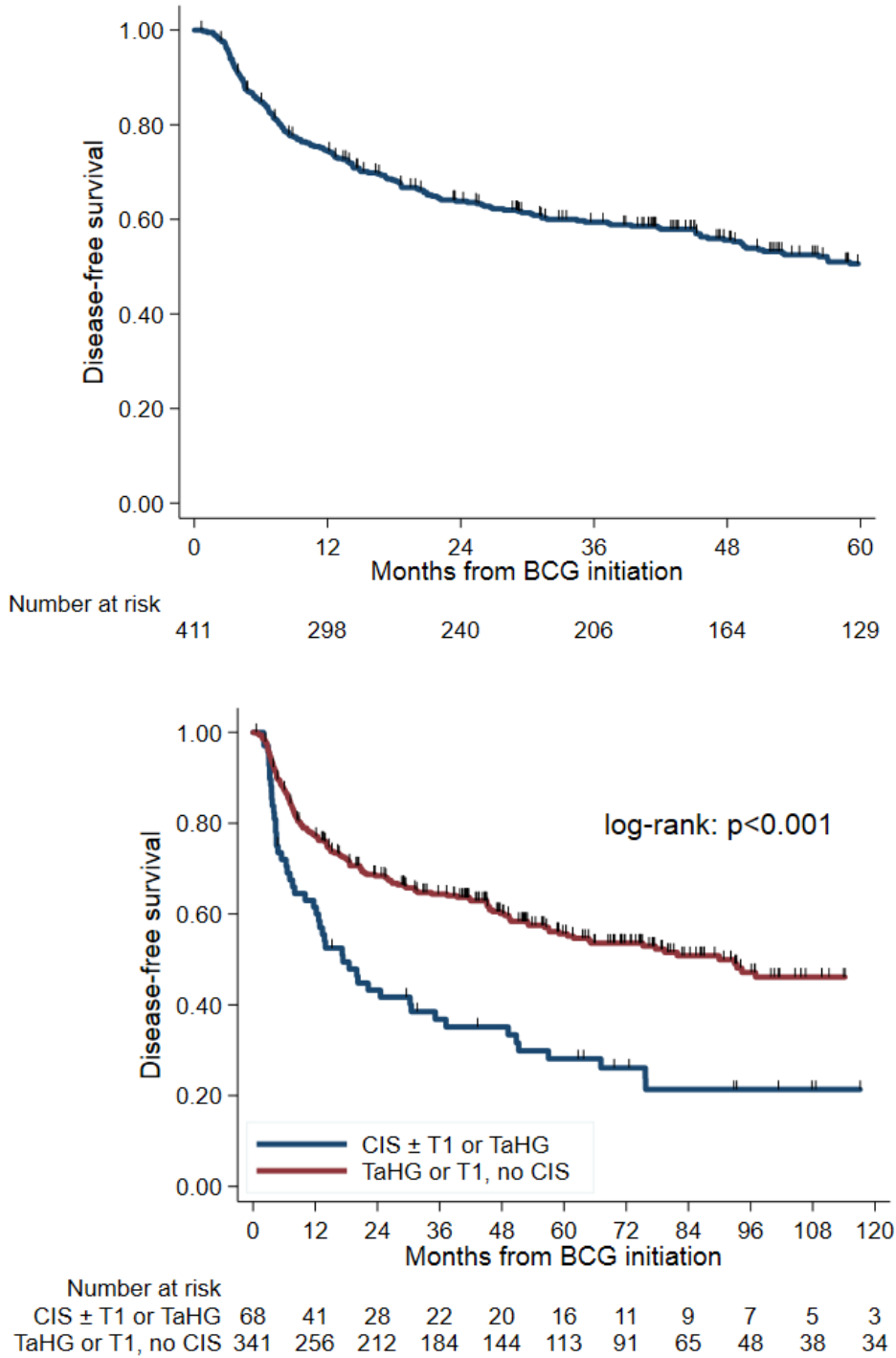
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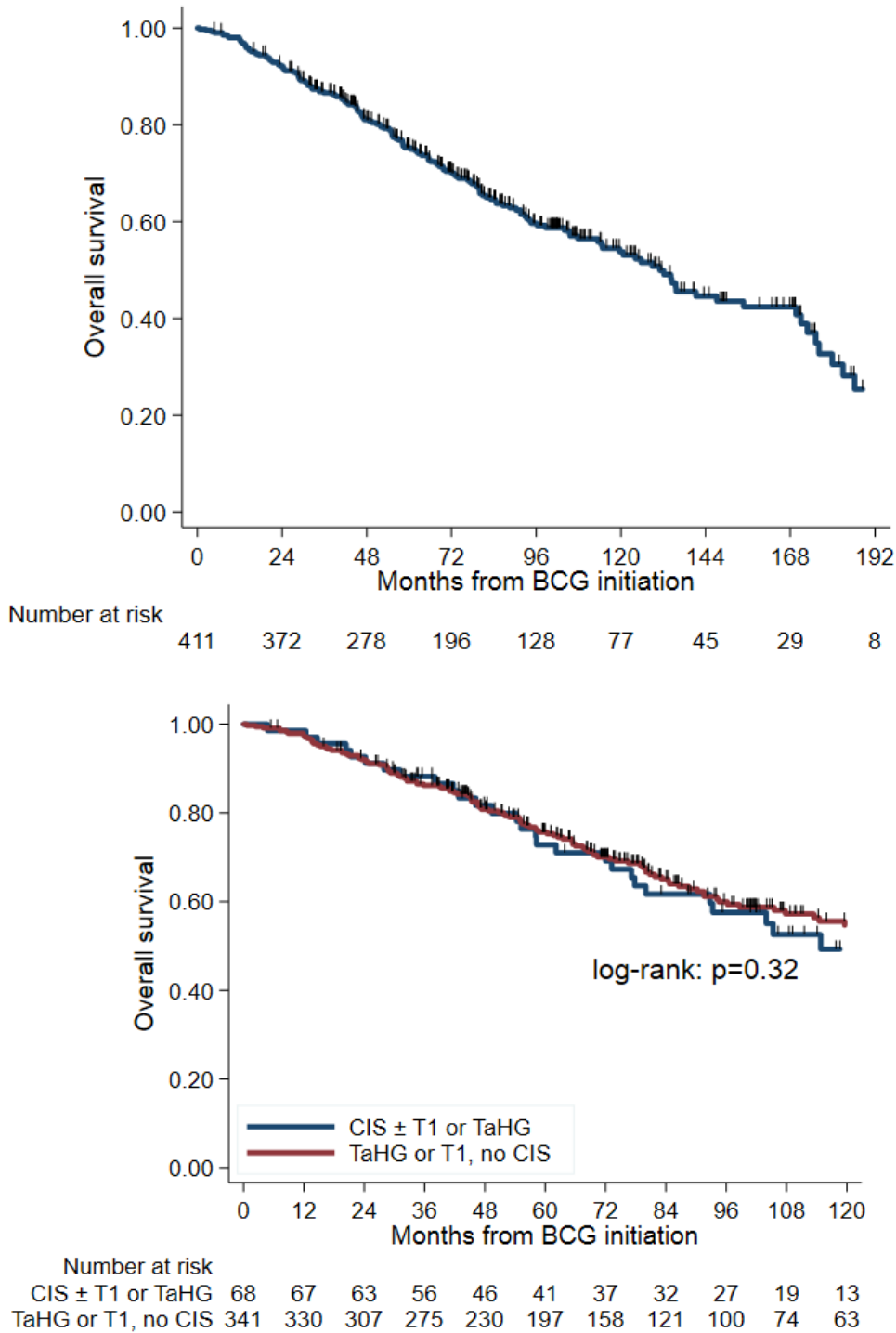
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This supplementary material has been provided by the authors to give readers additional information about their work.

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



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)		1.10 (0.75-1.60)	
Smoking			0.12		0.42
Current	63/145	Ref.		Ref.	
Former	111/199	1.37 (1.01-1.85)		1.25 (0.89-1.76)	
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	88.1%	83.5%	78.2%	73.9%
CIS ± T1 or TaHG	81.8%	66.8%	60.0%	-
TaHG or T1, no CIS	89.4%	86.9%	82.2%	78.6%
Cystectomy	93.0%	89.7%	88.1%	88.1%
CIS ± T1 or TaHG	87.7%	79.2%	75.6%	-
TaHG or T1, no CIS	94.0%	91.8%	90.7%	90.7%
Death	86.6%	75.3%	52.8%	30.5%
CIS ± T1 or TaHG	88.2%	72.8%	49.3%	-
TaHG or T1, no CIS	86.2%	75.7%	54.7%	36.8%
BC death	97.6%	94.7%	92.15%	85.0%
CIS ± T1 or TaHG	98.5%	89.0%	86.5%	-
TaHG or T1, no CIS	97.4%	95.9%	93.6%	86.3%

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 ¹	Odds Ratio (95% CI) ²	P-value ²
	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					

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

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

	Median (25 th percentile – 7 th percentile)		P-value ¹	Coefficient ²	P-value ²
	No Progression (N=330)	Progression (N=71)			
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 (49,108-18,3485)	<.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 th percentile – 7 th percentile)				
	No Progression (N=330)	Progression (N=71)	P-value ¹	Coefficient ²	P-value ²
² 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 (25th percentile, 75th percentile)

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