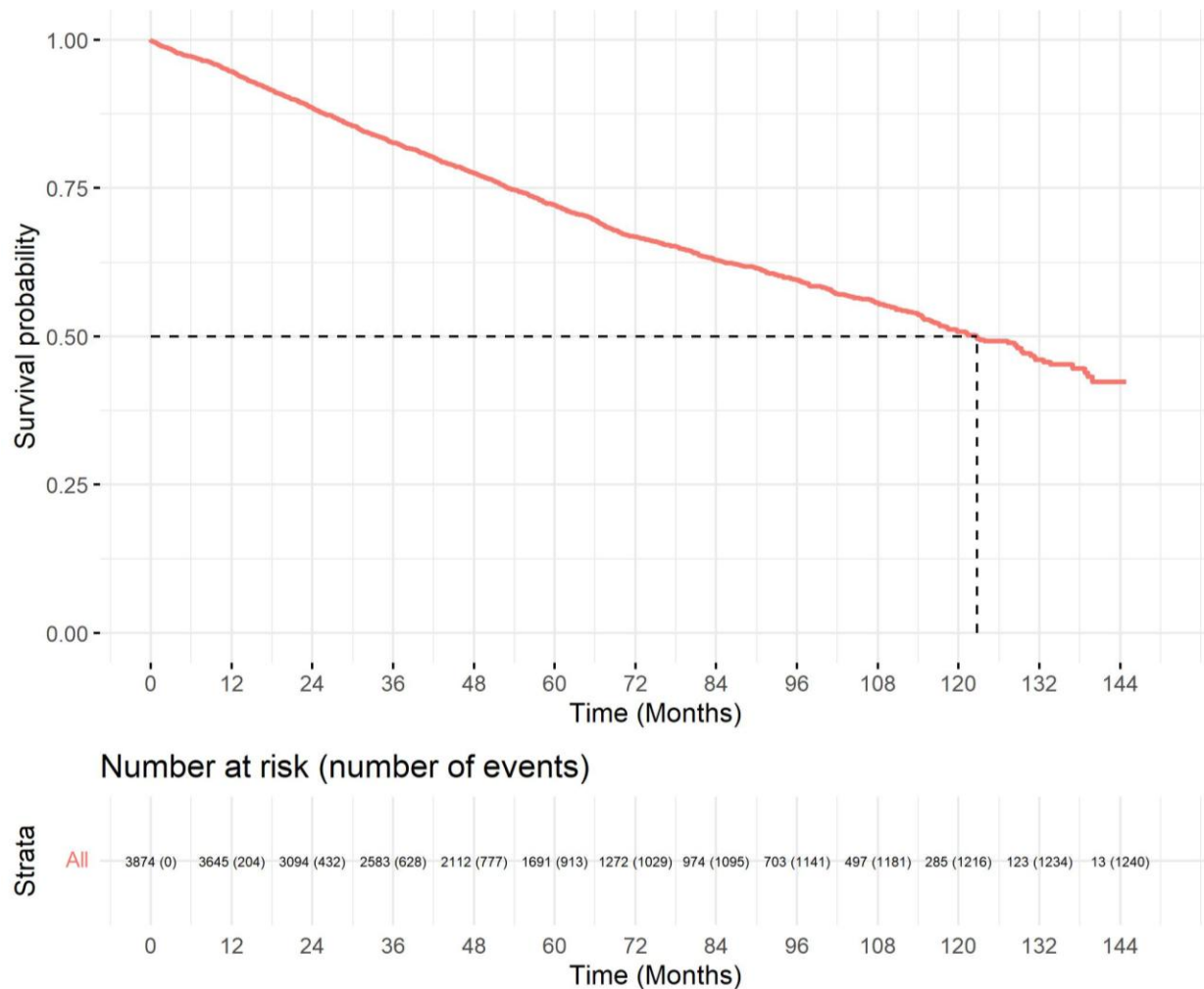


APPENDIX

Supplementary Figure 1. Overall survival from date of diagnosis among individuals with de novo HR-NMIBC diagnosed from 2010–2020 in Alberta, Canada. HR-NMIBC: high-risk non-muscle-invasive bladder cancer; OS: overall survival.



Characteristic	Median (Months)	12 Month	24 Month	60 Month
Overall	122.7 (116.4, 130.7)	0.947 (0.940, 0.954)	0.886 (0.875, 0.896)	0.722 (0.706, 0.738)

Gotto et al. A population-based analysis of patterns of care in patients with high-risk non-muscle invasive bladder cancer from Alberta, Canada.

Supplementary Table 1. Description of databases used
Alberta Cancer Registry (ACR):
Cancer is a reportable disease within the province of Alberta. The ACR captures information on all individuals diagnosed with cancer within the province of Alberta (200,000+ cases). This database also includes information related to cancer morphology and stage which are captured from pathology, physician, and laboratory reports, electronic medical records, along with patient charts. In addition, this database houses information on the date and cause of death along with the last known date of follow-up which are captured via vital statistics and the population registry. The database currently captures individuals diagnosed with cancer between 2004-2020 and has follow-up data until the end of 2020.
ARIA (Electronic Medical Records)
The ARIA database consists of electronic medical records for all 17 provincial cancer centers (2 tertiary centers, 4 regional and 11 community centers) covering 4.5 million residents of Alberta. This database contains information related to patient care including information on systemic therapies (including the date and dose of each agent within each cycle of each chemotherapy regimen), radiation therapy, treatment facility, and visits with cancer physicians (including specialty type).
Discharge Abstract Database (DAD):
The DAD database captures information for each instance where an individual has been discharged from an inpatient hospital bed. This database contains International Classification of Diseases, Tenth Revision – Canadian Enhancement (ICD-10-CA) diagnostic codes for the most responsible diagnosis and secondary diagnoses. Information is also captured on procedures that occurred during the hospitalization. Such procedures are coded according to the Canadian Classification of Health Interventions (CCI) system. In addition, information on the date and the duration of the hospitalization are also available as are information on aspects of patient costs such as the resource intensity weight. Data accuracy and quality are assessed on a regular basis by hospital administration and the Canadian Institute for Health Information (CIHI).
National Ambulatory Care Reporting System Database (NACRS):
The NACRS database captures information on all inpatient and outpatient use of ambulatory care services. This database contains ICD-10-CA diagnostic codes and the date of service. As with the DAD, data accuracy and quality are assessed on a regular basis by hospital administration and the Canadian Institute for Health Information (CIHI).
Practitioner Claims Database (PC):
The PC database captures physician and allied practitioner claims used for reimbursement and shadow-billing purposes that have been processed by the Alberta government. This database includes information such as the processed claim amount, diagnostic codes (ICD-9-CM: International Classification of Diseases, Ninth Revision – Clinical Modification), and health service codes (CCP: Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures).
Pharmaceutical Information Network Database (PIN):
The PIN database captures information on all prescription drugs dispensed from community pharmacies in the province. Information within the PIN database is collected from community pharmacists and includes information on the drug name, dose, and quantity dispensed. Complete

Gotto et al. A population-based analysis of patterns of care in patients with high-risk non-muscle invasive bladder cancer from Alberta, Canada.

information from this database is available starting in 2010. While data are available prior to 2010, these data are incomplete since they were collected prior to the enactment of regulations that mandated the collection of pharmacy dispensary records which occurred in 2007.

Variable	Source	Codes
BCG – TICE	PIN/ARIA	DIN (TICE): 02153513 – Merck ATC: L03AX03
BCG – Russian	PIN/ARIA	DIN (Russian): 02508613 – Verity Pharma
TURBT	Physician claims	69.2, 69.29
Radical cystectomy	Physician claims	69.51
Partial cystectomy	Physician claims	69.4, 69.4A
Gemcitabine	PIN/ARIA	DIN: 02402831, 02298783, 02318741, 02402831 ATC: L01BC05
Mitomycin C	PIN/ARIA	DIN: 02230451, 02464691 ATC: L01DC03

ARIA: Electronic medical records database; ATC: anatomical therapeutic chemical; BCG: bacillus Calmette-Guérin; DIN: drug identification number; PIN: Pharmaceutical Information Network Database; TURBT: transurethral resection of bladder tumor.

Year	Population	HR-NMIBC	
		Cases	Incidence (95% CI)
2010	3732082	286	7.7 (6.8-8.6)
2011	3789030	326	8.6 (7.7-9.6)
2012	3874548	335	8.6 (7.7-9.6)
2013	3981011	319	8.0 (7.2-8.9)
2014	4083648	350	8.6 (7.7-9.5)
2015	4144491	389	9.4 (8.5-10.4)
2016	4196061	417	9.9 (9.0-10.9)
2017	4241100	385	9.1 (8.2-10.0)
2018	4298275	367	8.5 (7.7-9.5)
2019	4361694	346	7.9 (7.1-8.8)
2020	4421876	354	8.0 (7.2-8.9)

CI: confidence interval; HR-NMIBC: high-risk non-muscle-invasive bladder cancer.

Gotto et al. A population-based analysis of patterns of care in patients with high-risk non-muscle invasive bladder cancer from Alberta, Canada.

Supplementary Table 4. Baseline characteristics of the NMIBC cohort, stratified by risk status, from Alberta, Canada from 2010–2020.					
Variable	Overall n=6837	HR- NMIBC n=3874	L/IR- NMIBC n=2963	p	SMD
Male, n (%)	5363 (78.4)	3181 (82.1)	2182 (73.6)	<0.001	0.205
Urban residence, n (%)	5679 (83.1)	3244 (83.7)	2435 (82.2)	0.095	0.041
Age at Dx, years, mean (SD)	69.7 (11.9)	71.4 (11.2)	67.6 (12.4)	<0.001	0.322
Age at Dx, years, median [IQR]	71.0 [62.0, 78.0]	72.0 [64.0, 80.0]	69.0 [60.0, 77.0]	<0.001	0.322
Age at Dx, categories, n (%)				<0.001	0.274
≤65	2344 (34.3)	1138 (29.4)	1206 (40.7)		
66–75	2170 (31.7)	1233 (31.8)	937 (31.6)		
≥76	2323 (34.0)	1503 (38.8)	820 (27.7)		
No. of Charlson comorbidities, n (%)				0.001	0.093
0	3672 (53.7)	2019 (52.1)	1653 (55.8)		
1	1952 (28.6)	1113 (28.7)	839 (28.3)		
≥2	1213 (17.7)	742 (19.2)	471 (15.9)		
T stage, n (%)				<0.001	2.019
T1	1934 (28.3)	1934 (49.9)	0 (0.0)		
Ta	4238 (62.0)	1275 (32.9)	2963 (100.0)		
Tis	665 (9.7)	665 (17.2)	0 (0.0)		
Tumor grade, n (%)				<0.001	5.479
High	3287 (48.1)	3287 (84.8)	0 (0.0)		
Low/intermediate	3205 (46.9)	242 (6.2)	2963 (100.0)		
Missing	345 (5.0)	345 (8.9)	0 (0.0)		
T stage + tumor Grade, n (%)				<0.001	1.573
T1 + high-grade	1732 (25.3)	1732 (44.7)	0 (0.0)		
T1 + low/int-Grade	99 (1.4)	99 (2.6)	0 (0.0)		
T1 + missing	103 (1.5)	103 (2.7)	0 (0.0)		
Ta + high-grade	1275 (18.6)	1275 (32.9)	0 (0.0)		
Ta + low/int-grade	2963 (43.3)	0 (0.0)	2963 (100.0)		
Tis + high-grade	280 (4.1)	280 (7.2)	0 (0.0)		
Tis + low/int-grade	143 (2.1)	143 (3.7)	0 (0.0)		
Tis + missing	242 (3.5)	242 (6.2)	0 (0.0)		
Year of diagnosis, n (%)				0.195	0.044
2010–2014	2821 (41.3)	1616 (41.7)	1205 (40.7)		
2015–2017	2074 (30.3)	1191 (30.7)	883 (29.8)		
2018–2020	1942 (28.4)	1067 (27.5)	875 (29.5)		

Dx: diagnosis; HR-NMIBC: high-risk non-muscle-invasive bladder cancer; IQR: interquartile range; Low/Int: low/intermediate; SD: standard deviation.

Gotto et al. A population-based analysis of patterns of care in patients with high-risk non-muscle invasive bladder cancer from Alberta, Canada.

Supplementary Table 5. Baseline characteristics of the HR-NMIBC cohort, stratified by type of first therapy, in Alberta Canada from 2010–2020.						
Variable	Overall	BCG	Gem/Mito	Neither	p	SMD
n	3874	1381	137	2356		
Male (%)	3181 (82.1)	1159 (83.9)	120 (87.6)	1902 (80.7)	0.011	0.126
Urban Residence (%)	3244 (83.7)	1063 (77.0)	111 (81.0)	2070 (87.9)	<0.001	0.193
Age at Dx, years, mean (SD)	71.4 (11.2)	70.0 (10.1)	70.1 (9.7)	72.3 (11.8)	<0.001	0.139
Age at Dx, categories (%)					<0.001	0.148
≤65	1138 (29.4)	444 (32.2)	43 (31.4)	651 (27.6)		
66–75	1233 (31.8)	489 (35.4)	49 (35.8)	695 (29.5)		
≥76	1503 (38.8)	448 (32.4)	45 (32.8)	1010 (42.9)		
No. of Charlson comorbidities (%)					0.001	0.106
0	2019 (52.1)	782 (56.6)	69 (50.4)	1168 (49.6)		
1	1113 (28.7)	372 (26.9)	39 (28.5)	702 (29.8)		
≥2	742 (19.2)	227 (16.4)	29 (21.2)	486 (20.6)		
T stage (%)					<0.001	0.274
T1	1934 (49.9)	718 (52.0)	92 (67.2)	1124 (47.7)		
Ta	1275 (32.9)	426 (30.8)	27 (19.7)	822 (34.9)		
Tis	665 (17.2)	237 (17.2)	18 (13.1)	410 (17.4)		
Tumor grade (%)					<0.001	0.238
High	3287 (84.8)	Suppressed	Suppressed	Suppressed		
Low/intermediate	242 (6.2)	Suppressed	Suppressed	Suppressed		
Missing	345 (8.9)	Suppressed	Suppressed	Suppressed		
Year of diagnosis (%)					<0.001	0.163
2010–2014	1616 (41.7)	578 (41.9)	62 (45.3)	976 (41.4)		
2015–2017	1191 (30.7)	491 (35.6)	36 (26.3)	664 (28.2)		

Gotto et al. A population-based analysis of patterns of care in patients with high-risk non-muscle invasive bladder cancer from Alberta, Canada.

2018–2020	1067 (27.5)	312 (22.6)	39 (28.5)	716 (30.4)		
-----------	----------------	------------	-----------	------------	--	--

The gemcitabine and mitomycin C categories were combined into a single group (Gem/Mito) to prevent the suppression of cells due to the limited number of individuals who received mitomycin C (n=24). Cells were marked “suppressed” to prevent the identification of strata <10. BCG: bacillus Calmette-Guérin; Dx: diagnosis; HR-NMIBC: high-risk non-muscle-invasive bladder cancer; IQR: interquartile range; SD: standard deviation.

Supplementary Table 6. Predictors of BCG initiation among individuals with HR-NMIBC diagnosed from 2010–2020 in Alberta, Canada						
Characteristic	Univariable			Multivariable		
	OR	95% CI	p	OR	95% CI	p
Age at diagnosis, Yrs						
≤65	—	—	—	—	—	—
66–75	1.03	0.87, 1.21	0.724	0.99	0.83, 1.19	0.944
≥76	0.67	0.57, 0.78	<0.001	0.67	0.56, 0.80	<0.001
Sex						
Female	—	—	—	—	—	—
Male	1.22	1.03, 1.45	0.026	1.13	0.94, 1.36	0.201
Residence						
Rural	—	—	—	—	—	—
Urban	0.47	0.39, 0.55	<0.001	0.49	0.40, 0.59	<0.001
No. of Charlson comorbidities						
0	—	—	—	—	—	—
1	0.79	0.68, 0.92	0.003	0.85	0.72, 1.00	0.057
≥2	0.70	0.59, 0.84	<0.001	0.76	0.62, 0.92	0.006
T Stage						
T1	—	—	—	—	—	—
Ta	0.84	0.73, 0.98	0.026	0.76	0.65, 0.88	<0.001
Tis	0.93	0.77, 1.11	0.408	1.25	0.98, 1.60	0.073
Tumor grade						
High	—	—	—	—	—	—
Low/intermediate	0.35	0.24, 0.48	<0.001	0.25	0.17, 0.36	<0.001
Diagnosed in						
2010–2014	—	—	—	—	—	—
2015–2020	0.89	0.80, 0.99	0.035	0.80	0.71, 0.90	<0.001

Notes: Individuals missing information on disease grade were excluded from the analyses (n=345; 8.9% of total cohort). OR <1 = decreased odds of BCG; OR >1 = increased odds of BCG. BCG: bacillus Calmette-Guérin; CI: confidence interval; Dx: diagnosis; Gr: grade; HG: high-grade; HR-NMIBC: high-risk non-muscle-invasive bladder cancer; Low/Int: low/intermediate; OR: odds ratio; Yr: year.