

Supplementary material for: Real-world cost-effectiveness of a policy of *KRAS* testing to inform cetuximab or panitumumab for third-line therapy of metastatic colorectal cancer in British Columbia, Canada

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Statements and Declarations

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Table S1 – Data sources and costing methods

Health resource	Resource data source	Cost data source
Hospitalization	Canadian Institute for Health Information (CIHI) Discharge Abstract Database[1]	CIHI Resource Intensity Weight method, using Cost of a Standard Hospital Stay for BC by year [2, 3]
Physician services	BC Medical Services Plan (MSP) fee-for-service physician claims [4]	Total paid amount available from BC MSP claims
Medical Oncologist services	BC Cancer Scheduling data [5]	Unit cost (hourly rate) calculated from negotiated service contract ranges [6]
Outpatient prescription drugs	BC PharmaNet dispensing records, including both private and public pay (BC PharmaCare) [7]	Total cost (ingredient cost, plus dispensing fee) available from PharmaNet dispensing records
Chemotherapy drugs	BC Provincial Systemic Therapy Program (PSTP) dispensing records [5]	Ingredient cost available from PSTP dispensing records; delivery cost (mean staff time) from BC Cancer internal data
Radiotherapy	BC Cancer Radiotherapy Data Warehouse [5]	Unit costs (planning costs, delivery cost per fraction, and follow-up cost) from Yong <i>et al</i> [8]
<i>KRAS</i> testing cost	BC Cancer Genetics and Genomics Lab (CGL) testing records [9]	Unit cost per test (CA\$250) provided by CGL

Table S2 – Balance statistics for sensitivity analysis for matching method

		UNADJUSTED COHORT			REDUCED GENMATCH			GREEDY MATCH			IPTW		
		Pre-policy N = 453	post-policy N = 1304	std. diff.	Pre-policy N = 453	post-policy N = 565	std. diff.	Pre-policy N = 453	post-policy N = 906	std. diff.	Pre-policy N = 453	post-policy N = 1304	std. diff.
Covariate		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)		%	%	
Age (years)	Mean ± SD	63.4 (10.3)	63.2 (10.8)	0.021	63.4 (10.3)	63.6 (10.2)	0.017	63.4 (10.3)	62.6 (10.6)	0.082	63.1 (21.4)	63.3 (12.4)	0.011
	Median (IQR)	64 (56-71)	64 (57-71)		64 (56-71)	64 (57-71)		64 (56-71)	64 (56-70)		64 (56-71)	64 (57-71)	
	Female	185 (40.8)	524 (40.2)	0.048	185 (40.8)	376 (41.5)	0.013	185 (40.8)	375 (41.4)	0.011	40.1	40.4	0.006
Colorectal cancer type	C18	302 (66.7)	787 (60.4)	0.148	302 (66.7)	521 (57.5)	0.193	302 (66.7)	599 (66.1)	0.041	60.8	61.7	0.022
	C19	28 (6.2)	98 (7.5)		28 (6.2)	78 (8.6)		28 (6.2)	60 (6.6)		7.1	7.1	
	C20	123 (27.2)	419 (32.1)		123 (27.2)	307 (33.9)		123 (27.2)	247 (27.3)		32.2	31.1	
Income Quintile	1 (lowest)	92 (20.3)	251 (19.3)	0.091	92 (20.3)	173 (19.1)	0.100	92 (20.3)	171 (18.9)	0.064	17.0	19.3	0.132
	2	92 (20.3)	238 (18.3)		92 (20.3)	188 (20.8)		92 (20.3)	175 (19.3)		21.0	18.5	
	3	81 (17.9)	279 (21.4)		81 (17.9)	189 (20.9)		81 (17.9)	184 (20.3)		17.5	21.2	
	4	90 (19.9)	269 (20.6)		90 (19.9)	185 (20.4)		90 (19.9)	186 (20.5)		22.5	20.4	
	5 (highest)	98 (21.6)	267 (20.5)		98 (21.6)	171 (18.9)		98 (21.6)	190 (21.0)		22.0	20.6	
Health Authority	Interior	107 (23.6)	305 (23.4)	0.124	107 (23.6)	217 (24.0)	0.057	107 (23.6)	206 (22.7)	0.057	24.2	23.8	0.0532
	Fraser	140 (30.9)	428 (32.8)		140 (30.9)	280 (30.9)		140 (30.9)	278 (30.7)		31.6	32.2	
	Vancouver Coastal	116 (25.6)	294 (22.6)		116 (25.6)	230 (25.4)		116 (25.6)	232 (25.6)		22.7	23.1	
	Vancouver Island	72 (15.9)	215 (16.5)		72 (15.9)	143 (15.8)		72 (15.9)	144 (15.9)		17.0	16.4	
	Northern	18 (4.0)	62 (4.8)		18 (4.0)	36 (4.0)		18 (4.0)	46 (5.1)		4.5	4.5	
	Rural residence	51 (11.3)	173 (13.3)	0.061	51 (11.3)	102 (11.3)	0.000	51 (11.3)	107 (11.8)	0.017	11.2	13.1	0.059
Charlson’s Score	0	339 (74.8)	940 (72.1)	0.075	339 (74.8)	678 (74.8)	0.000	339 (74.8)	692 (76.4)	0.066	73.1	72.8	0.000
	1	58 (12.8)	190 (14.6)		58 (12.8)	117 (12.9)		58 (12.8)	112 (12.4)		14.3	14.2	
	2+	28 (6.2)	78 (6.0)		28 (6.2)	56 (6.2)		28 (6.2)	49 (5.4)		5.8	6.0	
	Missing	28 (6.2)	96 (7.4)		28 (6.2)	55 (6.1)		28 (6.2)	53 (5.9)		6.8	7.0	
Days from diagnosis to eligibility date	Mean (SD)	1041 (844)	1079 (843)	0.045	1041 (844)	1103 (967)	0.068	1041 (844)	1012 (777)	0.036	1069 (1731)	1066 (966)	0.002
	Median (IQR)	802 (504-1292)	841 (515.5-1375.5)		802 (504-1292)	789 (511-1400)		802 (504-1292)	802 (508-1289)		801 (506-1353)	835 (514-1363)	
	Prior colorectal surgery	374 (82.6)	994 (76.2)	0.157	374 (82.6)	649 (71.6)	0.262	374 (82.6)	757 (83.6)	0.026	77.9	77.8	0.002
	Prior liver surgery	58 (12.8)	184 (14.1)	0.038	58 (12.8)	114 (12.6)	0.007	58 (12.8)	119 (13.1)	0.010	13.2	13.6	0.012
	Prior radiotherapy	150 (33.1)	460 (35.3)	0.046	150 (33.1)	362 (40.0)	0.142	150 (33.1)	293 (32.3)	0.016	36.1	35.0	0.024
	Prior bevacizumab	251 (55.4)	1035 (79.4)	0.529	251 (55.4)	504 (55.6)	0.004	251 (55.4)	649 (71.6)	0.342	73.7	73.4	0.007

TABLE S3 – MEAN AND MEDIAN SURVIVAL ESTIMATES BY POLICY PERIOD IN CRUDE (UNMATCHED) COHORT, BEFORE AND AFTER INTRODUCTION OF KRAS TESTING AND CETUXIMAB OR PANITUMUMAB TREATMENT

	Pre-policy		Post-policy	
	estimate (days)	95% CI	estimate (days)	95% CI
Mean	227	200-254	330	299-362
Median	129	112-144	155	145-169

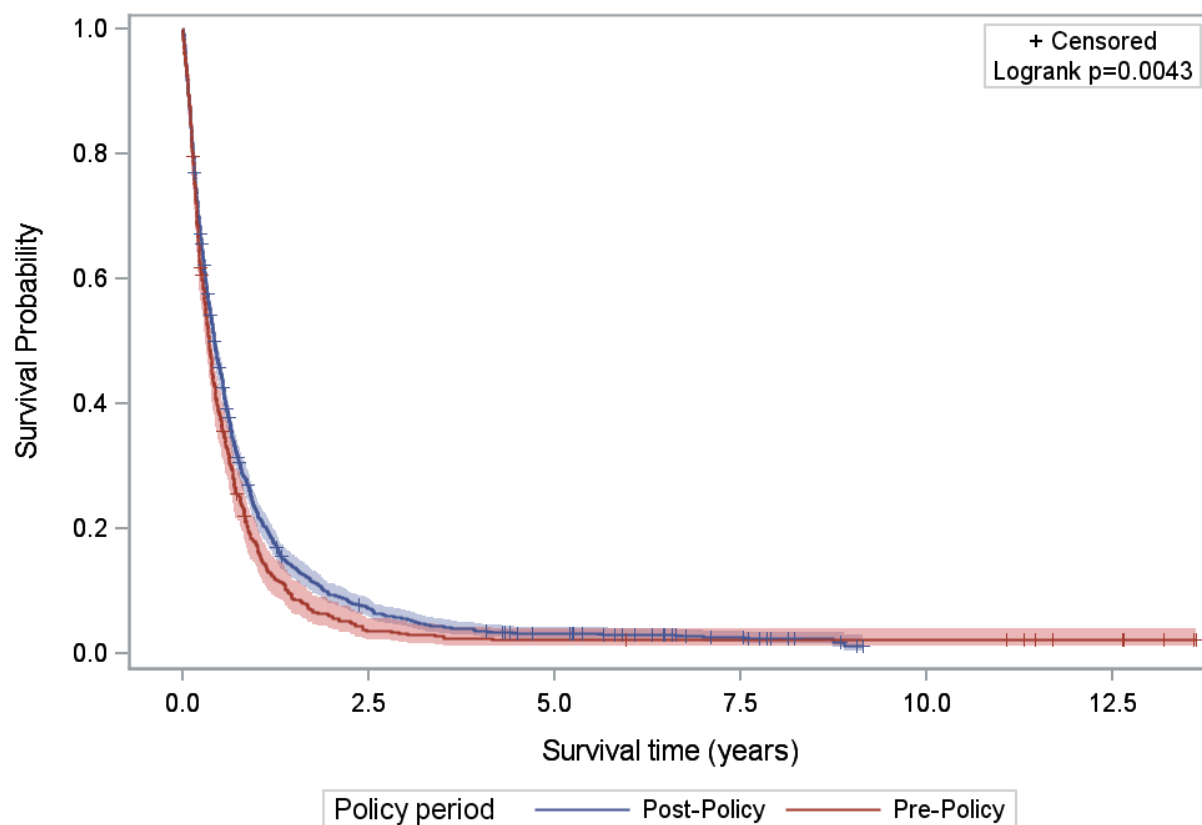


FIGURE S1 – OVERALL SURVIVAL BY POLICY PERIOD, BEFORE AND AFTER INTRODUCTION OF KRAS TESTING AND CETUXIMAB OR PANITUMUMAB TREATMENT, IN CRUDE (UNMATCHED) COHORT

Survival probability estimated using Kaplan-Meier method. Tick marks indicate censored cases. Shading indicates 95% confidence interval. Difference is statistically significant using the log-rank test.

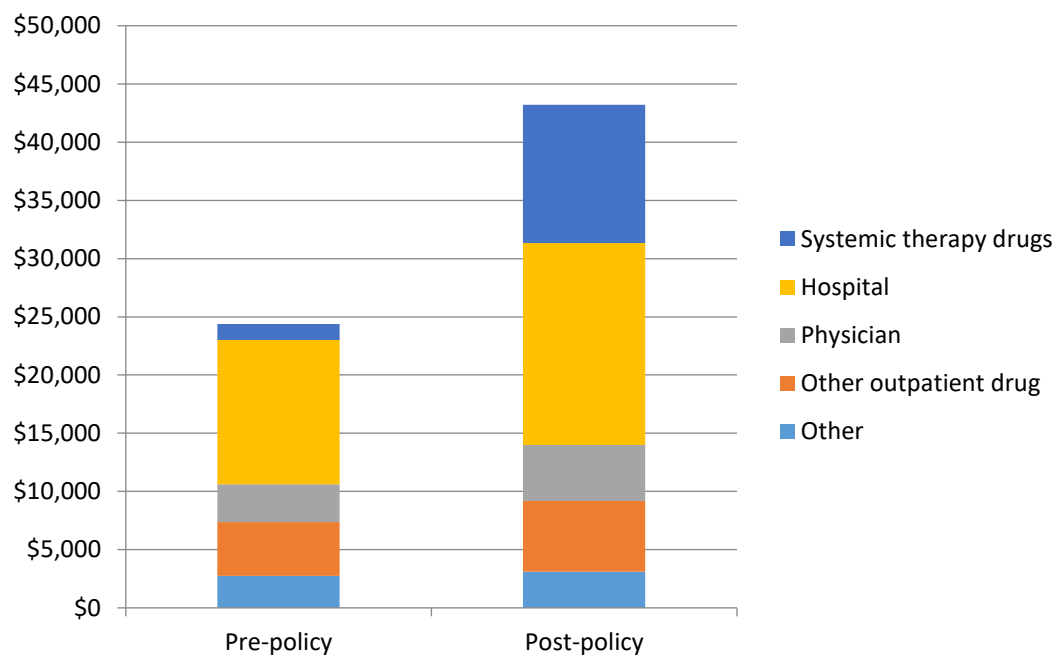


FIGURE S2 — AVERAGE COST PER PATIENT BY POLICY PERIOD AND HEALTH RESOURCE.

Costs expressed in 2020 Canadian dollars. Costs are calculated using an 8-year time horizon, adjusted for censoring using inverse-probability weighting, and discounted 1.5% per year. “Other” includes the cost of *KRAS* testing

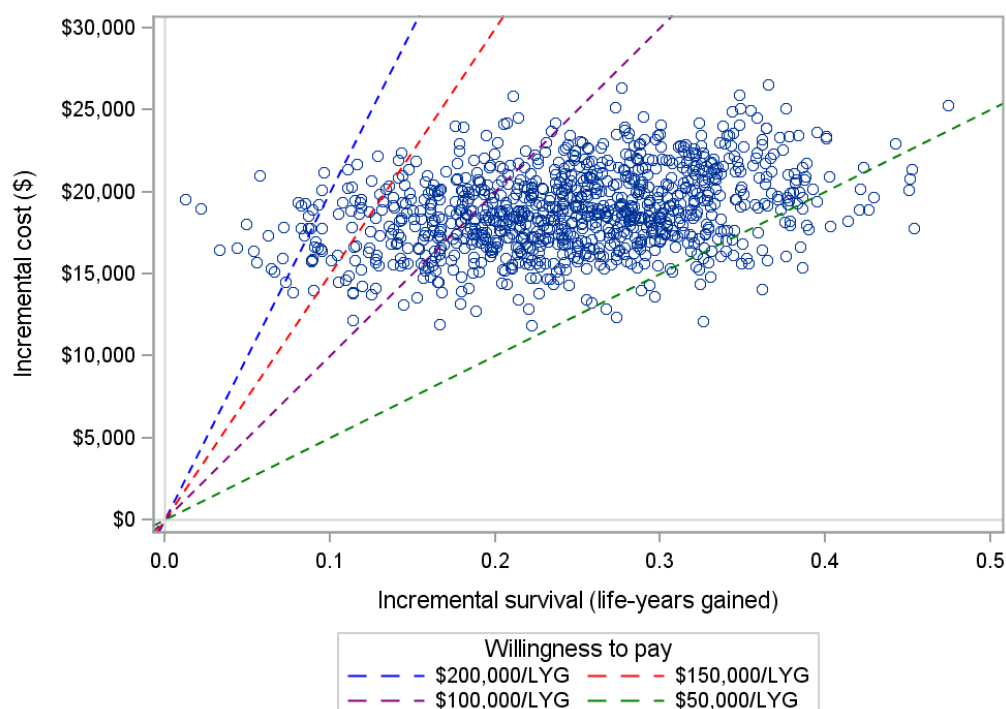


FIGURE S3 – SCATTER PLOT OF INCREMENTAL COST AND EFFECTIVENESS OF POLICY CHANGE

Each point represents results of one bootstrap sample (n=1000). Dashed reference lines show alternative threshold values

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