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Health Care Utilization and Costs in Lung Cancer Screening Participants—A Propensity-Matched Economic Analysis



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ABSTRACT

Introduction: Lung cancer screening (LCS) for high-risk populations has been firmly established to reduce lung cancer mortality, but concerns exist regarding unintended downstream costs.

Methods: Mean health care utilization and costs were compared in the Alberta Lung Cancer Screening Study in a cohort undergoing LCS versus a propensity-matched control group who did not.

Results: A cohort of 651 LCS participants was matched to 336 unscreened controls. Over the study period (mean 3.6 y), a modest increase in the number of claims (22.4 versus 21.9 per person-year [PY]; Δ 0.50 [95% confidence interval: 0.15-0.86], p = 0.006) and outpatient visits (4.01 versus 3.50 per PY; Δ 0.51 [0.37-0.65], p < 0.0001), but not in inpatient admissions, was noted in the screened cohort. Claims payments, inpatient costs, and cancer care costs were similar in the screening arm versus the unscreened. Outpatient encounter costs per participant were higher in the screened group (\$2662.18 versus \$2040.67 per PY; Δ -\$621.51 [-1118.05 to -124.97], p = 0.014). Removing the additional computed tomography screening examinations rendered differences not significant. Mean total costs were not significantly different at \$6461.10 per PY in the screening group and \$6125.31 in the unscreened group (Δ -\$335.79 [-2009.65 to 1338.07], p = 0.69).

Conclusions: Modest increases in outpatient costs are noted in individuals undergoing LCS, in part attributable to the screening examinations, without differences in overall

health care costs. Health care costs and utilization seem otherwise similar in individuals participating in LCS and those who do not.

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Keywords: Lung cancer; Screening; Low-dose CT scan; Cost analysis

Introduction

Screening individuals at high risk of developing lung cancer with low-dose chest computed

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tomography has been firmly established to reduce the mortality from this disease which remains the most common cause of cancer deaths internationally. The two largest randomized trials suggest that even short-term screening can reduce lung cancer-specific mortality by 20% to 24%. As many jurisdictions implement screening, focus on cost-effectiveness of the intervention is of substantial interest given the ever-escalating costs of health care interventions.

The literature on health system impacts of lung cancer screening (LCS) has produced variable estimates of cost-effectiveness from modeling studies.³ The impact of various program parameters has also been reported such as use of risk prediction models,^{4,5} the addition of smoking cessation programs,⁶ nodule management algorithms,⁷ and even the addition of cardiac risk reduction interventions.⁸ Real-world assessment of resource utilization for screening participants has also been reported, but not contrasted with similar unscreened individuals.^{9,10}

Concerns regarding unintended costs from LCS have also been raised. Because computed tomography (CT) screening images more than the lungs, other incidental findings¹¹ may be detected which require additional investigations with associated downstream resource requirements and costs even if these may not result in management changes. As such, we aimed to compare mean health care utilization and costs in a cohort undergoing LCS versus a propensity-matched control group who did not undergo LCS.

Materials and Methods

In the Alberta Lung Cancer Screening Study, individuals were considered for participation in a LCS trial with three annual low-dose CT (LDCT) scans. 14 Participants were recruited through a combination of media reports, social media advertising, and paper posters and pamphlets in community centers and primary care medical offices. Eligible participants met either National Lung Screening Trial criteria (aged 55-74 y; \geq 30 pack-year smoking history; quit \leq 15 y ago) or were aged 55 to 80 years with an estimated six-year lung cancer risk greater than or equal to 1.5% using a validated model (PLCOm2012).¹⁵ The study was approved by the Health Research Ethics Board of Alberta—Cancer Committee (protocol HREBA.CC-16-0496) and was registered in a clinical trial database (NCT02431962). Participants consented to allow access to health care utilization data for the five-year period after enrollment, even if they did not meet the enrollment criteria or decided against proceeding with the screening intervention.

Propensity Match

A propensity-matched (PM) case selection was extracted from 805 individuals enrolled in the LCS program (cases) and 930 who did not proceed with the screening (controls). The PM was performed with logistic regression, and parameters allowed up to three screening participants per matched control with a caliper size of 0.25 and without replacement while using age, sex, education level, ethnicity, family history of lung cancer, personal cancer history, chronic obstructive pulmonary disease (COPD) diagnosis, history of depression, smoking status, pack-years, number of years since quit, and body mass index as covariates. A higher ratio of screened:unscreened participant was selected as it was anticipated that many unscreened individuals would have a considerably lower risk of lung cancer which may also affect other comorbidities and health care utilization.

Health Care Utilization and Costing

Health care costs and utilization were extracted through Health Research Methods and Analytics of Alberta Health Services, the Provincial health care system in a single-payer health care environment. The data were extracted from the following four sources: the Alberta Health Care insurance Plan Health Service Provider Claims data set (claims); the Discharge Abstract Database for inpatient hospital admissions; the National Ambulatory Care Reporting System (NACRS) for outpatient encounters; and the Cancer Control Alberta cancer registry and electronic medical records.

Dates of data extraction were from the time of participant enrollment in the study (May 7, 2015, to August 11, 2017) to March 31, 2019, for physician claims, and October 31, 2019, for Cancer Control Alberta, Discharge Abstract Database, and NACRS. All health care encounters were included regardless of associated diagnosis.

Claims data included all claims by Alberta physicians working on a fee-for-service basis but excluded some physicians on salary or alternate payment plan programs (estimated as 16% of physicians and 11.5% of family physicians during the period of the study¹⁶). Physician costs were estimated based on actual costs paid using the Alberta-based fee-for-service (FFS) schedule of medical benefits.

Inpatient costs were estimated based on a case mix costing approach. This approach provides estimates on the average case mix group (CMG) and measures average resource use in index terms. Using the 2019 CMG data file sourced from the Alberta Health Interactive Health Data Application, ¹⁷ average cost per CMG was matched to the CMG values assigned to each inpatient stay. Inpatient costs included services provided in hospital for

admitted patients, such as activities supported by nurses, other professional staff, laboratory services, other diagnostic services, and the dispensing and administration of drugs.¹⁸

Outpatient costs were estimated using the Comprehensive Ambulatory Care Classification System (CACS), which divides cases into ambulatory interventions, direct diagnostic imaging, rehabilitation, clinic visits, or emergency department visits. Direct, indirect, and drug and supply costs are then estimated for each CACS classification. Using Alberta-specific average cost estimates provided in the 2019 CACS data file available through the IHDA, average costs were matched to CACS codes available in the outpatient visit data. 18 Not included in the costing were outpatient prescription medications. As part of the research study, a group of screening participants had LDCT scan examinations performed in a contracted private facility which would not be included in the NACRS data set. The costs of these additional scans and count of outpatient encounters were added to participants accordingly using the NACRS payment rate although the actual contracted cost paid through the research was lower.

Cancer care-related visit costs we calculated based on the 2019 Alberta-based FFS schedule of medical benefits for the given specialty type. Chemotherapy treatments were calculated based on the Alberta Drug Benefit List for 2019 or from the Canadian Drug and Technology Agency pan-Canadian Oncology Drug Review cost recommendations. Radiation therapy treatment cost was calculated on a per fraction basis as previously described.¹⁹

Costs were summarized annually from year of study enrollment for each individual and compared between groups by number of person-years of follow-up data available adjusting for any mortality before the data extraction date. All cost values were price adjusted to 2021 Canadian dollars using the Bank of Canada inflation calculator. Costing methods are consistent with guidance provided by the Canadian Agency for Drugs and Technologies in Health. A secondary analysis of outpatient encounters and total costs was performed removing the cost of the three annual CT examinations (but not additional scans for follow-up of abnormal screens) to estimate potential costs associated with screening beyond the CT examinations themselves.

Management recommendations for LDCT incidental findings were driven by the interpreting radiologists. Efforts to follow consensus recommendations for such findings, such as the American College of Radiology white paper series, were encouraged and facilitated by synoptic reporting features in the screening system.²² Minor findings not requiring specific action could be

mentioned in the body of the imaging report, whereas those requiring action were also included in the summary section of the report. Coronary calcifications qualitatively described as moderate or severe were deemed actionable. Participants with actionable incidental findings were advised to have these reviewed with their primary care providers.

Statistical Analysis

Data analysis was performed with the SPSS statistics version 28 software (IBM Corporation, Chicago, IL) and the PM with add-on version 3.0.2.²³ Baseline cohort characteristics pre- and post-PM were performed with a two-sample independent t-test or Pearson's chi-square test. Rates of discrete events and associated annual and total costs per person-year of follow-up were calculated in the PM cohorts for each of physician claims, cancer care, outpatient and inpatient visits, and overall and compared between the two groups, and 95% confidence intervals (CIs) were calculated for the differences with the chi-square statistic for event rates and ttest for mean costs.²⁴ Diagnostic categories for physician claims (International Classification of Diseases, ninth revision [ICD-9]), outpatient encounters (International Classification of Diseases, tenth revision [ICD-10] and CACS), and inpatient admission (ICD-10 and CMG) were described in a descriptive format for the most frequently occurring categories.

Results

The PM sampling procedure provided for a cohort of 651 screening participant cases matched to 336 individuals who did not undergo screening for the control group. Baseline characteristics for the original and PM cohorts are outlined in Table 1. Significant differences in characteristics were found between the baseline cohort of screened and unscreened individuals. After the PM sampling, significant differences remained only in packyears of smoking and diagnosis of COPD, both slightly higher in the screening cohort. No covariate exhibited a large imbalance, and the propensity score (PS) distribution and standard differences pre- and post-matching are found in Supplementary Figure 1 as is the RGRAPH of each covariate distribution pre- and post-PM with improvements as expected.

The participants enrolled in the study between May 2015 and August 2017 with no difference in median length of follow-up from time of enrollment to data extraction (or death if earlier) between the two groups (screened: 1429 d, unscreened 1427 d, p=0.239). Furthermore, 11 of the screening participants (1.7%) died during the follow-up period versus nine in the control group (2.7%) (p=0.296).

	Full Cohort				Propensity-Matched Cohort			
Characteristic	All Participants (N = 1735)	Screening Group (n = 805)	Unscreened Group (n = 930)	p Value ^a	All Participants (N = 987)	Screening Group (n = 651)	Unscreened Group (n = 336)	p Value ^a
Age (mean ± SD)	62.1 ± 7.4	63.4 ± 6.2	61.0 ± 8.1	<0.001	62.8 ± 6.7	63.1 ± 6.2	62.3 ± 7.4	0.072
Sex (%female)	45.8	49.3	42.7	0.006	47.7	48.4	46.4	0.559
Smoking status (% current)	35.2	46	25.8	< 0.001	44	46.1	39.9	0.063
Smoking (pack-years)	31.7 ± 18.4	42.6 ± 15.6	22.2 ± 15.2	< 0.001	38.5 ± 15.9	40.7 ± 16.0	34.1 ± 14.7	< 0.001
Education level (%)				< 0.001				0.934
Less than high school graduation	8.2	10.7	6.1		9.6	10	8.9	
Post high school training	16.7	19	14.6		18.1	18.4	17.3	
Post high school training	16	18	14.2		17.4	17.2	17.9	
Some college	21.1	19.6	22.4		20.3	20.1	20.5	
College grad	25.6	21.7	29		23.2	22.1	24.7	
Postgrad-professional	12.4	10.9	13.7		11.3	11.8	10.4	
Race or ethnicity (%)				0.517				0.587
White	95.9	96.3	95.6		96.1	96.2	96.1	
Black	0.3	0.2	0.1		0.2	0.2	0.3	
Hispanic	0.3	0.2	0.3		0.2	0.3	0	
Asian	1.9	1.4	2.4		1.5	1.2	2.1	
Indigenous	1.6	1.9	1.3		1.9	2.2	1.5	
Family history of lung cancer (% yes)	25.9	28.4	23.7	0.023	27.7	28.4	26.2	0.459
Personal history of cancer (% yes)	18.1	19.8	16.7	0.096	20.3	20.1	20.5	0.878
Body mass index (mean kg/m ² \pm SD)	27.9 ± 5.2	27.7 ± 4.9	28.1 ± 5.4	0.147	27.7 ± 5.1	27.6 ± 5.0	27.8 ± 5.2	0.594
ECOG status (%)				0.006				0.087
0	80.1	77.1	82.6		79.6	79.1	80.7	
1	17.8	20.6	15.3		17.9	18.7	16.4	
2	2	2.2	1.7		2.1	2.2	0.21	
3	0.2	0	0.4		0.3	0	0.9	
History of depression (% yes)	22.7	23	22.5	0.801	23.6	23.2	24.4	0.672
Diagnosis of COPD (% yes)	18.7	11.8	6.9	<0.001	22.1	24.6	17.3	0.009
Chest symptoms (% yes)	14.8	14.7	14.8	0.917	15.5	14.6	17.3	0.404

Note: Bold results are those reaching statistical significance ($p \le 0.05$).

Table 1 Baseline Cohort Characteristics

COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group.

^aTwo-sample independent *t*-test or Pearson's chi-square test, screening group versus unscreened group.

Table 2. Frequency of Claims, Outpatient and Inpatient Events								
Event Type	Screening Group (n = 651)		Unscreen	ed Group (n $=$ 336)				
	Events	Events/Person-Year (95% CI)	Events	Events/Participant (95% CI)	Difference (95% CI), p Value			
Physician claims	44,119	22.4 (22.2-22.6)	22,001	21.9 (21.6-22.2)	0.50 (0.15-0.86), 0.006			
Outpatient visits	9194	4.01 (3.93-4.10)	4095	3.50 (3.40-3.61)	0.51 (0.37-0.65), < 0.0001			
Inpatient visits	295	0.13 (0.11-0.14)	161	0.14 (0.12-0.16)	-0.01 (-0.03 to 0.02), 0.49			

CI. confidence interval.

Resource Utilization and Diagnostic Categories

Frequency of claims and outpatient and inpatient events are detailed in Table 2. Over the study period, a modest increase in the number of claims (22.4 versus 21.9 per person-year [PY]; difference 0.50 [95% CI: 0.15-0.86], p = 0.006) and outpatient visits (4.01 versus 3.50 per PY; difference 0.51 [0.37–0.65], p < 0.0001), but not in inpatient admissions (0.13 versus 0.14 per PY; difference -0.01 [-0.03 to 0.02], p = 0.49), was noted in the screened cohort. ICD-9 codes associated with claims are outlined for both groups in Supplementary Table 1. Malignant neoplasm of the trachea or lung (162.x) was noted in 278 (0.63%) versus 62 (0.28%) of all claims in the screened and unscreened groups (p < 0.0001).

ICD-10 and CACS codes accounting for at least 0.5% of outpatient encounters are outlined in Supplementary Tables 2 and 3. Radiological examinations (ICD-10 Z01.6) and CT imaging (CACS) codes were more frequent in the screening group representing 20.9% versus 10% and 18.1% versus 4.8% of visits, respectively, or an additional 1940 CT examinations (2.98 examinations per participant, in line with the three annual LDCT performed for the research). Removing these additional CT examinations resulted in screened individuals revealing a lower number of outpatient visits (11.1 versus 12.2; difference -1.0[-1.2 to -0.6], p < 0.001). No differences in other diagnostic imaging tests (minor imaging, magnetic resonance imaging, or nuclear medicine imaging) were noted.

ICD-10 and CMG codes accounting for at least 0.5% of inpatient encounters are outlined in Supplementary Table 4. Lung cancer (ICD-10 C34.x) represented 5.4% versus 1.8% of admission diagnoses. CMG categories relating to lung cancer resection surgery represented 4.7% versus 1.2% of admission categories.

Health Care Costs

Cost data are detailed in Table 3. No statistically significant differences in claim payments per personyear were noted in any follow-up year nor overall. Across the entire follow-up period, claims payments were \$1941.19 per PY in the screening arm and \$1956.97 in the unscreened cohort (difference \$15.78 [-249.06 to 280.62], p = 0.91).

Mean outpatient encounter costs were higher in the screened group in years 3 and 5, including overall (\$2662.18 versus \$2040.67 per PY; difference -\$621.51 [-1118.05 to -124.97], p = 0.014). Removing the cost of the three annual CT examinations resulted in no significant differences between the groups (\$2308.62 versus \$2040.67; difference -\$267.95 [-776.16 to -240.26], p = 0.3).

Mean cancer care costs were similar between the groups on an annual basis and overall (\$224.19 versus \$175.31 per PY; difference -\$48.88 [-301.91 to 204.15], p = 0.70).

Mean inpatient admission costs were similar between the groups on an annual basis and overall (\$1907.12) versus 2228.59 per PY; difference \$321.47 [-\$730.33 to \$1373.27], p = 0.55).

Mean total costs inclusive of screening examinations were not significantly different between the groups, measured at \$6461.10 per PY in the screening group and \$6125.31 in the unscreened group (difference -\$335.79 [-2009.65 to 1338.07], p =0.69). Removing the cost of the three additional CT examinations reduced the screening group total cost to less than for the unscreened group numerically, although not statistically significant (\$5994.34 versus \$6125.31 per PY; difference \$130.97 [-1543.33 to 1805.37], p = 0.88).

Discussion

Our study compared health care utilization in a cohort of individuals undergoing LCS annually for three examinations with a propensity-matched group who did not. We found no overall differences in total health care costs over an average of 3.6 years of follow-up. A small increase in physician claims was noted in the screening group, as were increased outpatient visits and costs. The increased outpatient resource requirements were in part, but not entirely, accounted for by the LDCT examinations themselves. Some of these excess costs may relate to additional CT examinations required for some individuals beyond the three annual screens for follow-up of abnormalities.

Event Type and Year	Screening Group (n $=$ 651)		Unscreened G	roup (n = 336)		
	Cost per Person-Year (\$)	95% CI; SD	Cost per Person-Year	95% CI; SD	Difference (95% CI)	p Value
Physician claims						
Year 1	1809.76	1659.19-1960.34; 2006.60	1984.93	1719.82-2250.04; 2463.23	175.17 (-111.23 to 461.57)	0.23
Year 2	2004.36	1812.20-2196.52; 2465.19	2050.12	1750.68-2349.55; 23653.31	45.76 (-1791.65 to 1883.17)	0.96
Year 3	1973.56	1753.10-2194.03; 3609.40	1948.88	1689.11-2208.65; 3335.94	-24.68 (-488.52 to 439.16)	0.92
Year 4	2042.11	1743.47-2340.74; 4718.35	1507.48	1243.19-1771.77; 2292.29	-534.63 (-1069.73 to 0.47)	0.05
Total	1941.19	1804.53-2077.86; 1946.76	1956.97	1754.27-2159.67; 2124.80	15.78 (-249.06 to 280.62)	0.91
Outpatient encounters						
Year 1	2349.90	2026.48-2673.31; 4263.05	1967.16	1576.72-2357.59; 3635.23	-382.74 (-917.99 to 152.51)	0.16
Year 2	2836.58	2438.87-3234.28; 5157.87	2153.99	1695.75-2612.22; 7329.87	-682.59 (-1471.62 to 106.44)	0.09
Year 3	3195.97	2749.56-3642.37; 5604.04	2319.19	1797.97-2840.42; 4646.41	-876.78 (-1575.14 to -178.42)	0.014
Year 4	2125.51	1706.72-2544.30; 4709.35	1655.92	1264.92-2046.93; 3166.87	-469.59 (-1029.57 to 90.39)	0.1
Year 5	1723.86	273.59-3174.12; 6619.22	260.72	6.31-515.13; 609.88	-1463.14 (-2173.49 to -752.79)	0.0001
Total	2662.18	2332.21-2992.15; 4170.22	2040.67	1740.67-2340.68; 2824.31	-621.51 (-1118.05 to -124.97)	0.014
Total (without	2308.62	1943.20-2674.04; 4291.04	2040.67	1740.67-2340.68; 2824.31	-267.95 (-776.16 to 240.26)	0.3
3 screening CT)						
Cancer costs						
Year 1	264.96	50.80-479.13; 2919.63	235.01	-23.59 to 493.61; 2398.95	-29.95 (-392.93 to 333.03)	0.87
Year 2	223.91	-83.23 to 531.05; 3973.78	65.87	-55.16 to 186.90; 1116.15	-158.04 (-592.13 to 276.05)	0.48
Year 3	197.84	37.41-358.27; 2232.88	44.27	-32.95 to 121.50; 633.38	-153.57 (-397.58 to 90.44)	0.22
Year 4	203.83	5.72-401.94; 2858.08	455.29	-80.38 to 990.95; 4302.15	251.46 (-199.15 to 702.07)	0.27
Year 5	9.59	-9.61 to 28.79; 59.58	-	-	-	-
Total	224.19	85.00-363.38; 2130.71	175.31	12.36-338.25; 1422.95	-48.88 (-301.91 to 204.15)	0.7
Inpatient admissions						
Year 1	182.65	-2.31 to 367.62; 3247.97	589.97	-8.03 to 1187.96; 7478.90	407.32 (-245.01 to 1059.65)	0.22
Year 2	602.61	213.87-991.35; 5029.58	1104.65	279.60-1929.70; 7609.09	502.04 (-293.09 to 1297.17)	0.22
Year 3	298.27	112.44-484.10; 2203.48	626.96	15.38-1238.55; 22380.60	328.69 (-1407.92 to 2065.30)	0.71
Year 4	420.74	69.45-772.04; 3847.50	682.58	-228.58 to 1613.74; 7076.99	271.84 (-410.60 to 954.28)	0.43
Year 5	-		-		-	-
Total	1907.12	1370.65-2443.60; 8009.47	2228.59	1617.84-2839.34; 7919.83	321.47 (-730.33 to 1373.27)	0.55
All costs	6461.10	5553.01-7368.90; 13,342.03	6125.31	5137.16-7113.46; 11,344.86	-335.79 (-2009.65 to 1338.07)	0.69
All costs (without 3 screening CT)	5994.34	5063.49-6925.19; 13,346.90	6125.31	5137.16-7113.46; 11,344.86	130.97 (-1543.33 to 1805.27)	0.88

Note: Mean costs are per participant per person-year, in 2021 Canadian dollars. Bold results are those reaching statistical significance ($p \le 0.05$). CI, confidence interval; CT, computed tomography.

Our findings are similar to those from an analysis of National Lung Screening Trial Medicare participants which found no differences between the LDCT and chest radiograph arm of the trial. This study although larger and randomized did not include an unscreened arm, so that increased costs in both screening arm versus no screening could not be excluded. The results suggest that incidental findings unrelated to lung cancer do not have significant downstream impacts on health care costs and utilization.

Our study did not randomize individuals to a screening or no-screening arm but rather used a propensity-based matching approach. Although this statistical technique can match individuals based on known and available covariates, unknown or unavailable covariates may exist making the groups different in other characteristics, which may affect health care utilization. Nevertheless, our matching resulted in very similar groups in terms of age, body mass index, educational status, and with slightly higher smoking and COPD rates in the screening cohort which would likely result in higher health care needs and bias costestimates in favor of the unscreened group.

The short-term analysis performed may introduce biases increasing the relative cost of screening versus no screening. The stage shift from early detection would lead to earlier treatment costs but prevent more expensive lung cancer treatment at a future date beyond the time frame of our analysis. 19 We did find more lung cancer surgery-related inpatient admissions in the screened cohort as one would expect from an early detection program. An argument could be made that some of these early lung cancers represent overdiagnosis; longer term studies suggest that overdiagnosed lung cancers are a very small fraction of screening detected cases.²⁷ Other potential added benefits of screening such as increased tobacco cessation²⁸ and cardiac risk modifications⁸ would also likely accrue benefits in a longer-term horizon. The assigned health care system costs used was that of a standard diagnostic CT examination which is likely higher than the true cost of a noncontrast LDCT examination. Nevertheless, because the screening was coordinated from a screening research study, no LCS programmatic costs were included in our measurements.

Some potentially important health care costs were missing from our data set, such as some non-FFS physician claims, private diagnostic imaging examination, and community laboratory testing. Nevertheless, we have no reason to believe that either cohort would have different proportion of non-FFS physicians or more utilization of private imaging services (uncommon in this health care system). Our sample size was relatively small, and, in some cases, wide CIs around difference

between the groups may have masked differences with potential economic implications. Our costs and utilization rates also reflect those of a universal and publicly funded Canadian health care environment and associated practice patterns. These may not apply to other health care jurisdictions or systems. Finally, management protocols for incidental findings could affect downstream costs, and the ideal approach to this component of LCS remains unknown.

In conclusion, health care costs and utilization seem similar in individuals participating in LCS and those who do not. Concerns about important increased downstream costs of screening could not be detected in our analysis.

CRediT Authorship Contribution Statement

Alain Tremblay: Principal investigator for the ALCSS. Responsible for original conception and design of the work, data analysis and interpretation, drafting of the manuscript and final approval. Agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Shainur Premji: Contributed to data acquisition, analysis and interpretation, critical review of the manuscript, and final approval. Agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Nguyen Xuan Thanh: Contributed to data analysis and interpretation, critical review of the manuscript, and final approval. Agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Huiming Yang: Contributed to data interpretation, critical review of the manuscript, and final approval. Agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Paul MacEachern: Co-investigator for the ALCSS. Contributed for original conception and design of the work, data interpretation, critical review of the manuscript, and final approval. Agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at https://doi.org/10.1016/j.jtocrr.2023.100594.

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